ARCHIVES OF OTOLARYNGOLOGY

OLUME 43 JANUARY 1946 NUMBER 1

COPYRIGHT, 1946, BY THE AMERICAN MEDICAL ASSOCIATION

IRRADIATION OF THE EUSTACHIAN TUBE

AN ANATOMIC, PHYSICAL AND CLINICAL STUDY OF A TREATMENT FOR RECURRENT OTITIS MEDIA APPLIED TO AERO-OTITIS

MAJOR EDMUND P. FOWLER JR.
MEDICAL CORPS, ARMY OF THE UNITED STATES

Exposure of the eustachian tube to radon, dium or roentgen ray will often prevent recurnt otitis media when this condition is due excess lymphoid tissue about the pharyngeal tium of the eustachian tube.[1] It is particurly valuable for certain cases of otitis media e to barotrauma (aero-otitis). This comunication will concern itself with some of the roblems which have been encountered in irradiion of the eustachian tubes of airmen. As to current otitis media and deafness in other roups, the value of the treatment has already en established by Crowe, Burnam and their o-workers.[2]

The known susceptibility of lymphoid tissue irradiation is the basis for the use of radiation the nasopharynx. This susceptibility was first served in lymph nodes, but experience has own that adenoid tissue is quite as sensitive. his has been confirmed by Schenck [3] on biopsy terial. It is remarkable how little radiation required to produce a profound effect (fig. 1). fter one treatment, the germinal centers roughout the specimen have disappeared, and e number of lymphocytes is greatly reduced. any of those which remain have pyknotic clei. The capillaries in the irradiated tissue e prominent. Their endothelium is thickened d their walls are hyalinized. Connective tissue lls are much more prominent than in the control biopsy specimen (fig. 2). The aviator from whom these biopsy specimens were taken sustained marked relief from his aero-otitis and his "scratchy" throat after one radium treatment.

There is considerable difference of opinion as to the amount of lymphoid tissue which is normally present in and about the eustachian tube. This has caused controversy as to the theoretic value of different types of radiation. For this and other reasons, various types of filtration have been used for radon and radium, while some radiotherapeutists have suggested that high voltage roentgen therapy should be employed.

A review of the anatomy and the pathology of the eustachian tube must be made before it can be decided which variation in radiation technic is most desirable. It is necessary to determine the absorption characteristics of various filters in relation to beta and gamma radiation and the expected dose at the various depths that have been found by anatomic study to be of importance. To be of value the method must be readily available, free from danger and convenient for both patient and physician.

When excess lymphoid tissue is seen about the torus tubarius and there is improper function of the tube, it has been assumed that the lymphoid tissue is responsible.[2] The best basis for this belief has been the clinical observation that irradiation of the mouth of the tube reduces the lymphoid tissue that may be present, and this usually is followed by an improvement in the function of the tube. The improvement can be demonstrated by using a manometer with the Valsalva maneuver (Perlman [4]). If the otitis is long-standing and severe, transudates disappear from the middle ear and deafness is diminished. Furthermore, airmen subjected to conditions which require especially good function of the tubes are able to fly again after the treatment.[5] They can also withstand severe

The temporal bone material in this paper was pre- red in paraffin by Staff Sergeant M. Bressler under direction of Lieutenant Colonel D. Murray Angevine, C., in a general medical laboratory in the European heater of Operations.

1. Fowler, E. P., Jr.: Non-Surgical Treatments for eafness, Laryngoscope **52**:204 (March) 1942.

2. (*a*) Crowe, S. J., and Baylor, J. W.: The Prevenon of Deafness, J. A. M. A. **112**:585 (Feb. 18) 1939. (*b*) Crowe, S. J., and Burnam, C. F.: Recognition, reatment and Prevention of Hearing Impairment in hildren, Ann. Otol., Rhin. & Laryng. **50**:15 (March) 941. (*c*) Crowe, S. J.; Guild, S. R.; Langer, E.; och, W. E., and Robbins, M. H.: Impaired Hearing in chool Children, Laryngoscope **52**:790 (Oct.) 1942.

3. Schenck, H. P.: Influence of Nasopharyngeal Hyerplasia on the Ear, Laryngoscope **51**:780 (Aug.) 1941.

4. Perlman, H. B.: Eustachian Tube: Abnormal Patency and Normal Physiologic State, Arch. Otolaryng. **30**:212 (Aug.) 1939.

(Footnotes continued on next page)

tests in the pressure chamber, so that the treatment should also be applicable to submarine crews and deep sea divers.

The literature is neither voluminous nor specific about the location of the lymphoid tissue in and around the eustachian tube. "Gerlach's tonsil" (gross lymphoid tissue in the cartilaginous part of the tube) is always mentioned, but there is considerable question whether this is ever a normal structure, even in children. Gerlach's only observation of it was in a 6 month old child. No statement is made in either of his

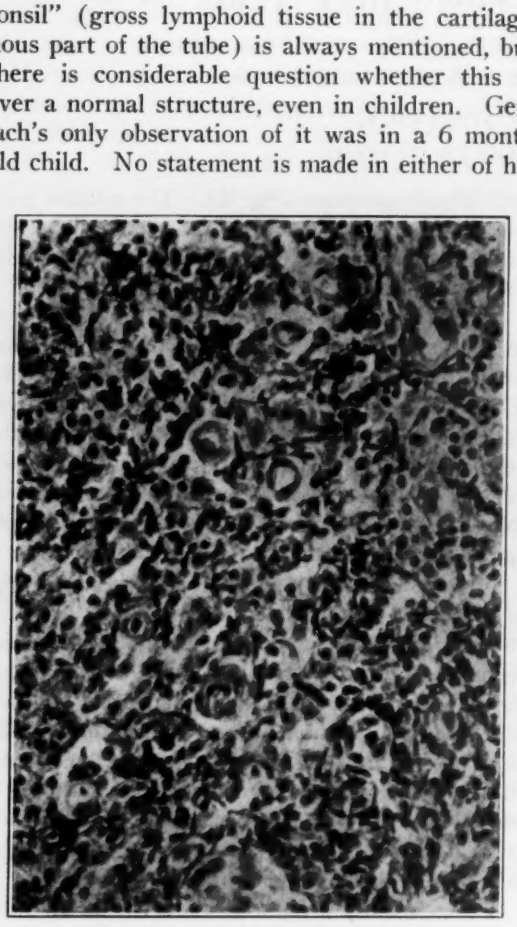


Fig. 1.—Lymphoid tissue from the salpingopharyngeal fold of a young aviator, taken one month after 50 milligram hours' exposure to radium contained in a platinum capsule with a 0.5 mm. wall. The biopsy specimen was taken approximately 1 cm. from the site of the capsule. Note the absence of germinal centers and the prominence of the endothelium of capillaries. Magnification, × 375.

articles as to whether the middle ear was normal. There may well have been a history of otitis media or of low grade eustachian salpingitis. Wolff [7] in examining 500 temporal bones from 250 persons of all ages found a circumscribed no of lymphoid tissue between the isthmus the mouth only once. Again it was in a 6 m old infant. Teutleben and Zöllner [8] descr such tissue in adults but concluded that wh is present it is pathologic.

Fig. 2.—Lymphoid tissue taken before treatment f a portion of the salpingopharyngeal fold of the s aviator as that shown in figure 1. Note the germ center and the relative insignificance of the capill and the connective tissue as compared with thos figure 1. Magnification, × 375.

Full length sections are occasionally sh from infantile or embryonal material, but authors have reported on histologic mate covering the entire length of the eustachian t of the adult. Wolff [9] published one article which conclusions were derived from study two completely sectioned adult temporal bo one horizontal, the other vertical. How m temporal bones in her series of 500 mentio in the foregoing paragraph showed the phar geal orifice, she does not say, but few collecti show the tube much beyond the isthmus in rout sections, even those from children. Graves a

5. Fowler, E. P., Jr.: Radon Treatment for Otitis Due to Barotrauma, J. Laryng. & Otol. **58**:489 (Dec.) 1943; Use of Radon to Prevent Otitis Media Due to Hyperplasia of Lymphoid Tissue and Barotrauma (Aero-Otitis), Arch. Otolaryng. **40**:402 (Nov.) 1944.

6. Gerlach: Zur Morphologie der Tuba Eustachii, Sitzungsb. d. phys.-med. Soc. zu Erlangen **2**:7, 1874; Monatschr. f. Ohrenh. **9**:49, 1875.

7. Wolff, D.: Microscopic Anatomy of the Eustachian Tube, Ann. Otol., Rhin. & Laryng. **43**:483 (June) 1934.

8. von Teutleben, E.: Die Tuben-Tonsille des M schen, Ztschr. f. Anat. u. Entwcklngsgesch. **2**:298, 1 1877. Zöllner, F., cited by Roy, D.: Frequency Effect on Eustachian Tube of Residual Lymphoid Ti in the Nasopharynx, Arch. Otolaryng. **24**:325 (Se 1936.

9. Wolff, D.: Microscopic Observation of the Eus chian Tube, Ann. Otol., Rhin. & Laryng. **40**:1 (Dec.) 1931.

wards [10] wrote of a "lymphoid layer" in the achian tube, but their detailed description cerns an embryo. Farrior,[11] after a study of) histologic sections of tube," stated that ere is no lymphoid tissue in or about the nor- eustachian tube."

n civilian life it is extremely difficult to obtain mal anatomic material from the respiratory t. In war it is possible to obtain specimens n young adults which give a proper anatomic kground for therapy. Material from airmen d in action substantiates the statements of e who believe that infection is the cause of presence of lymphoid tissue in the eustachian e and of any excess about its mouth. This so as to preserve not only the mastoid process, the middle ear and the labyrinth but also the entire length of the eustachian tube and the adjacent portions of the nasopharynx. This material shows that nasopharyngeal lymphoid tissue is common in American airmen in England. The tissue covers the torus tubarius in many airmen who never had enough aero-otitis to report to their group surgeon. It can be seen bumpily protruding from the torus tubarius and both the salpingopharyngeal and the salpingopalatine fold in about a third of the gross specimens examined. It was abundant posteriorly in about one half of the specimens. Lymphoid tissue tends to make the pharyngeal

Fig. 3.—Eustachian tube and the adjacent nasopharynx of an airman who had recurrent nasopharyngitis but never ical aero-otitis. Note adenoids and lymphoid tissue on the torus tubarius. Swollen lymphoid tissue in the areas icated by the arrows is most commonly the tissue to block the eustachian tube. Magnification, × 6.5. United tes Army Medical Museum neg. no. 82362.

terial suggests that lymphoid tissue is rarely undant enough to block the tube except at the opharyngeal orifice, precisely where it is iest to attack the tissue with radium (fig. 3). In the European Theater of Operations 95 rs of temporal bones have been removed from d airmen and examined grossly preparatory microscopic study. Eight pairs of bones have n removed from ground personnel of the same e group. Most of the bones were removed orifice of the tube a narrow slit, to which mucus adheres. One wonders if it is not thick mucus in a narrow opening which is the final lock in many nonfunctioning eustachian tubes. Many airmen have been found to have excess lymphoid tissue and no complaints of aero-otitis. Others get along well until they contract a slight "cold" with a postnasal drip. It is noteworthy that those who can fly with nasopharyngitis rarely have excess lymphoid tissue about the lips of the eustachian orifices.

To date, 1 bone from each of 16 persons has been cut and stained so as to allow analysis of the microscopic appearance of the entire length

10. Graves, G. O., and Edwards, L. F.: The Eustaan Tube, Arch. Otolaryng. **39**:359 (May) 1944.
11. Farrior, J. B.: Histopathologic Considerations in eatment of Eustachian Tube, Arch. Otolaryng. **37**: (May) 1943.

of the tube. Most interesting is the low grade eustachian salpingitis which is present in 11 of the 16 (fig. 4). Whether this is reaction to the English climate or to flying is difficult to say. Two of the temporal bones did not belong to airmen. They were from patients with debilitating diseases, and both showed slight eustachian salpingitis. Two temporal bones from members of the ground force who died of gunshot wounds showed none. Much more material must be examined before the incidence of eustachian salpingitis is known.

Fig. 4.—Vertical section of the eustachian tube of the same airman as that shown in figure 3, near the isthmus. Note the low grade salpingitis manifested by round cell infiltration and hyalinization of the submucosa (most marked in one of the rugae); also, exudation into the lumen. Note that the lumen is patent. Magnification, × 28. United States Army Medical Museum neg. no. 82613.

The salpingitis manifests itself by round cell infiltration, edema and often hyalinization of the submucosa. Hyperplasia of the lining epithelium and hypersecretion of the mucous glands are also usually present (fig. 5). The round cell infiltration becomes more and more extensive as infection progresses and eventually may i single germinal centers and sometimes masse lymphoid tissue with multiple centers. lymphoid tissue appears to push through the columnar ciliated epithelium covering it. A ally the highly organized ciliated epithel sloughs away, leaving a few areas covered undifferentiated low cuboidal epithelium (fig and 7). This is very similar to the pathol changes found in the bronchi and the paran sinuses with chronic infection (Semenov).[12] is even more striking in the eustachian t because there is less possibility of artefacts b produced in the specimens by brushing away delicate superficial parts of the ciliated thelium. The tube is so narrow and deep the lumen is protected from mechanical inj

Lymphoid masses are rare except near pharyngeal orifice but may occur anywhere a the length of the eustachian tube. If a chr infection is present, lymphoid tissue may o anywhere along the tube and even in the mi ear. Figure 6 shows some lateral to the isthm The occurrence of lymphoid tissue far from pharyngeal orifice of the tube makes one won if such tissue is not present in the airmen w do not receive benefit from radium in the n pharynx. Hyperplastic mucous membrane f or rugae, such as are shown in figures 4 and also may be responsible for failure of the tr ment. These may become edematous and p poid and so block the tube mechanically. I tant tissue will not be much affected by radi nor will polypoid tissue.

The complete or partial clinical records 80 airmen who had been treated with radon radium were available for this study. Airm are subjected to violent changes in pressure, a if they do not have normally functioning tub this is quickly apparent during descent or asce That 46 of the 80 airmen with recurrent ae otitis from various causes are known to ha returned to full flying duty after radiation tre ment is of significance. This means that in per cent of all the cases there was marked i provement. Some of the men who were lost follow-up observation may also have improv

The cases were selected because the patie had recurrent attacks of aero-otitis whi grounded them. A few had little excess lymp old tissue about the pharyngeal end of the eust chian tube, but in most of them it was pron nent. Many did not receive a full course

12. Semenov, H.: Personal communication to t author. Kistner, F.: The Histopathology and Bac riology of Sinusitis, Arch. Otolaryng. **13**:225 (Fe 1931.

atment, and many had complicating factors addition to whatever excess lymphoid tissue s present. For example, several had severe usitis or nasopharyngitis which in itself essitated return to the United States and refore discontinuance of the treatment. Four- n of the 80 airmen received only one treat- nt or were lost to observation after two. less a record of improvement was obtained y were considered unimproved. Of the 66 ients who received two or more treatments d were followed, 46, as mentioned, returned full flying duties. This means that 69 per cent those properly selected, treated and followed tained relief from symptoms. All had been unded repeatedly, and few were expected finish their tours.

aero-otitis. The others were free from symptoms, although they had all been grounded repeatedly before the treatments. None of the patients knew that an experiment was being performed, and the doctors had no idea at first which patient was being treated and which was not. After several weeks it was apparent that one group was doing well and the other badly. This small control series should answer the queries of those who wondered if the effect of putting radium capsules in the nose is not largely psychic.

In any discussion of irradiation it is essential to describe in deail the applicators used and in particular the amount of filtration employed. The patients described were treated with two types of platinum applicators, one sort containing

Fig. 5.—Eustachian salpingitis near the middle of a tube. Note the collections of lymphocytes (arrows) and e hyperactive glands. Magnification, × 25.

There seemed to be a possibility that the use radium might have a psychic effect on the atient; therefore it was decided to do a certain umber of control experiments on airmen. ummy capsules identical with the therapeutic apsules were supplied at two different hospitals arked so that no one could tell which set was aded and which was not. This was done so at the observation of the examiners would not e biased. Of the 34 alternate airmen, 17 were eated with 50 milligram hours of radium to ach side and 17 were treated with the placebos. our of the 17 treated with the placebos returned o flying duty, but only 1 returned without ymptoms. Thirteen of 17 alternate airmen who eceived the active capsules returned to full fly- ng duty. Two of the 13 had occasional mild

radon and the other radium element. The earlier patients were treated with a platinum applicator having a wall 0.65 mm. thick and containing radon. The later patients were treated with capsules having a wall 0.5 mm. thick and containing radium sulfate. The difference of dose between 0.5 mm. and 0.65 mm. of platinum is less than 5 per cent. The earlier patients were treated with 33 milligram hours to each side of the nasopharynx, and it was found that four to six treatments at three week intervals were necessary to obtain the desired effect. The later patients received 50 milligrams to each side of the nasopharynx for two to four treatments at four week intervals. These have been called respectively 66 and 100 milligram hours to the *whole* nasopharynx in previous communications.[4]

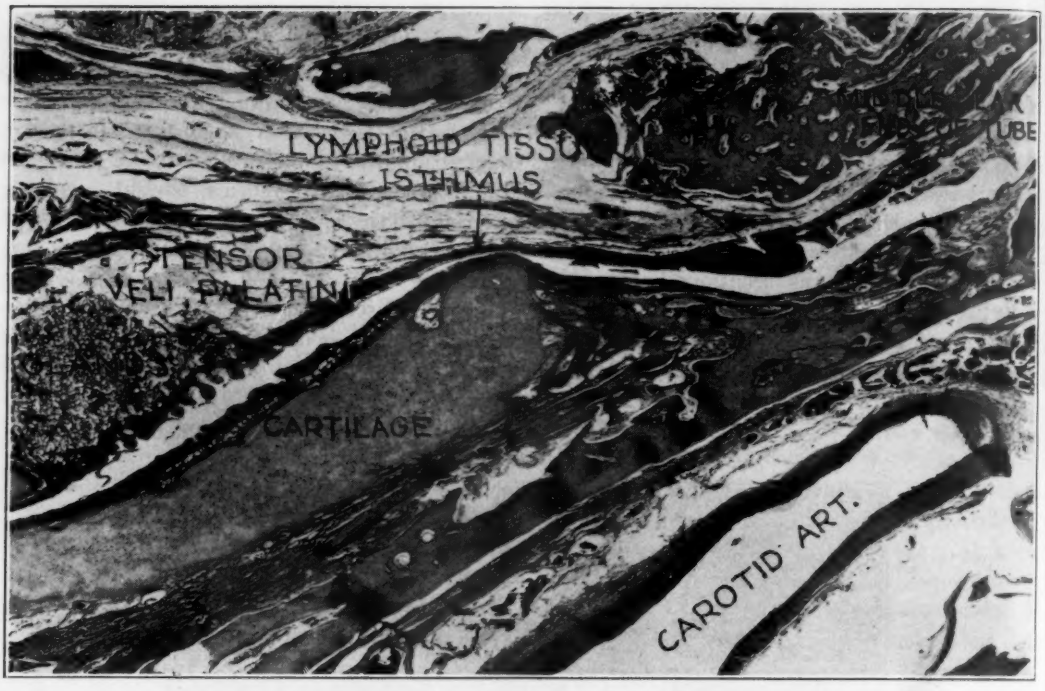


Fig. 6.—Section of the eustachian tube taken at an angle of 30 degrees to the horizontal. Note the inverted shape and the lymphoid mass lateral to the isthmus. Such findings are very rare in this position. Magnificati × 9. United States Medical Museum neg. no. 82360.

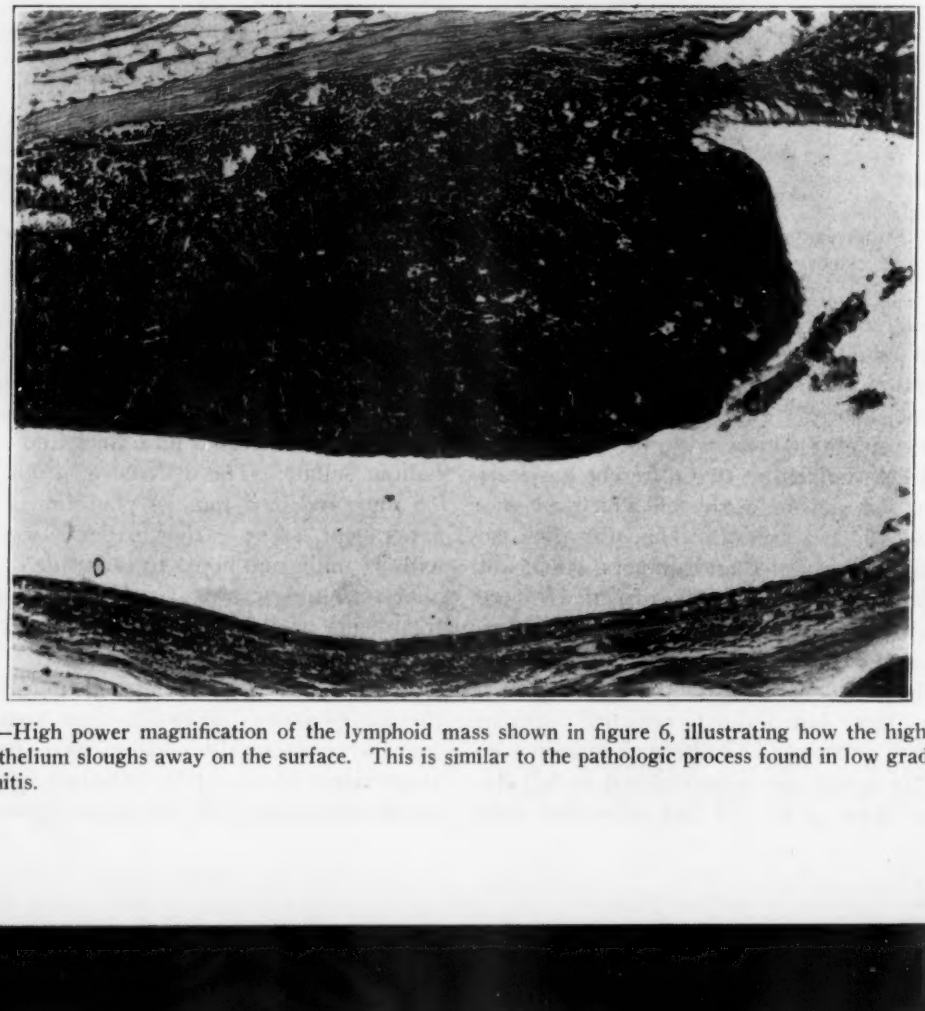


Fig. 7.—High power magnification of the lymphoid mass shown in figure 6, illustrating how the high columna ciliated epithelium sloughs away on the surface. This is similar to the pathologic process found in low grade sinusit and bronchitis.

ignation for *each side* of the nasopharynx is re accurate. The amount of radiation across nasopharynx is negligible (see the table and 8).

The capsules were 15 mm. long and had 3 mm. outside diameter. The effective length was 12.5 mm. (fig. 9). When filled with radon, each contained 75 millicuries of gas on delivery.

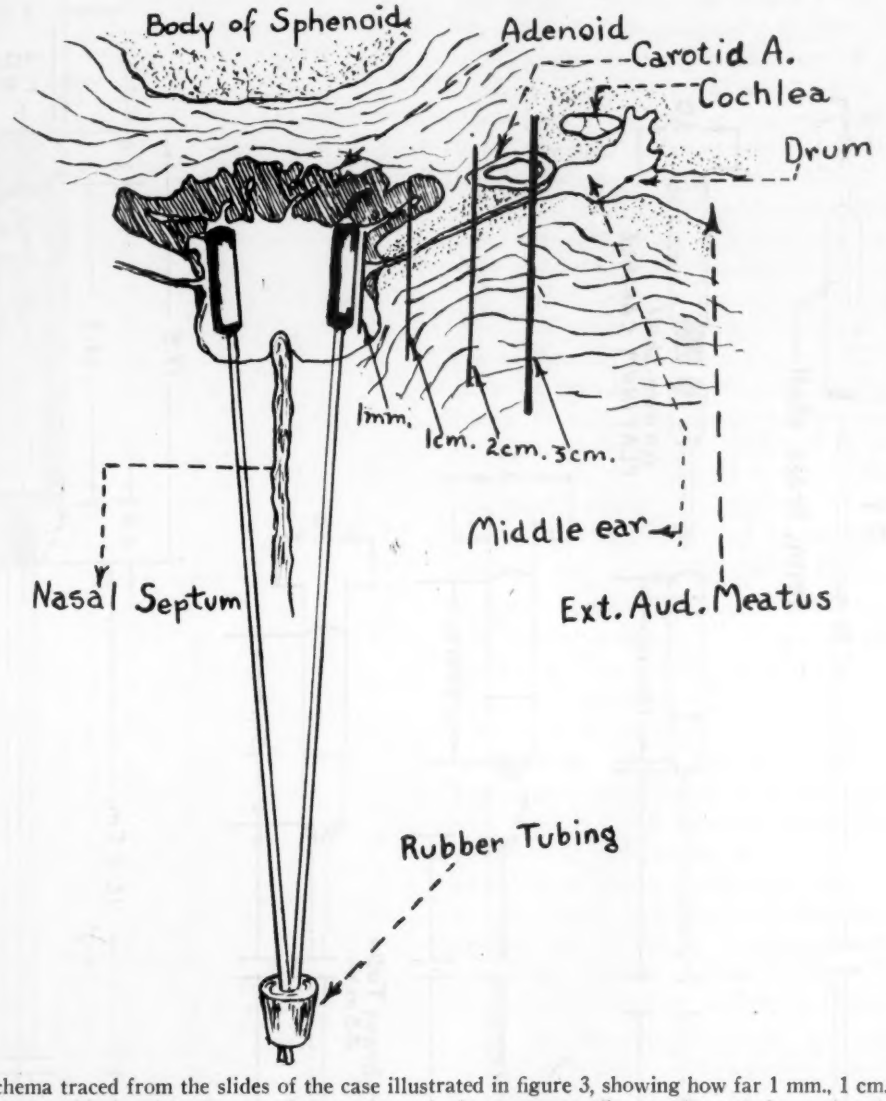


Fig. 8.—Schema traced from the slides of the case illustrated in figure 3, showing how far 1 mm., 1 cm., 2 cm. and m. is from a capsule placed in the nasopharynx through the nose according to the technic employed by me for diation of the eustachian tube.

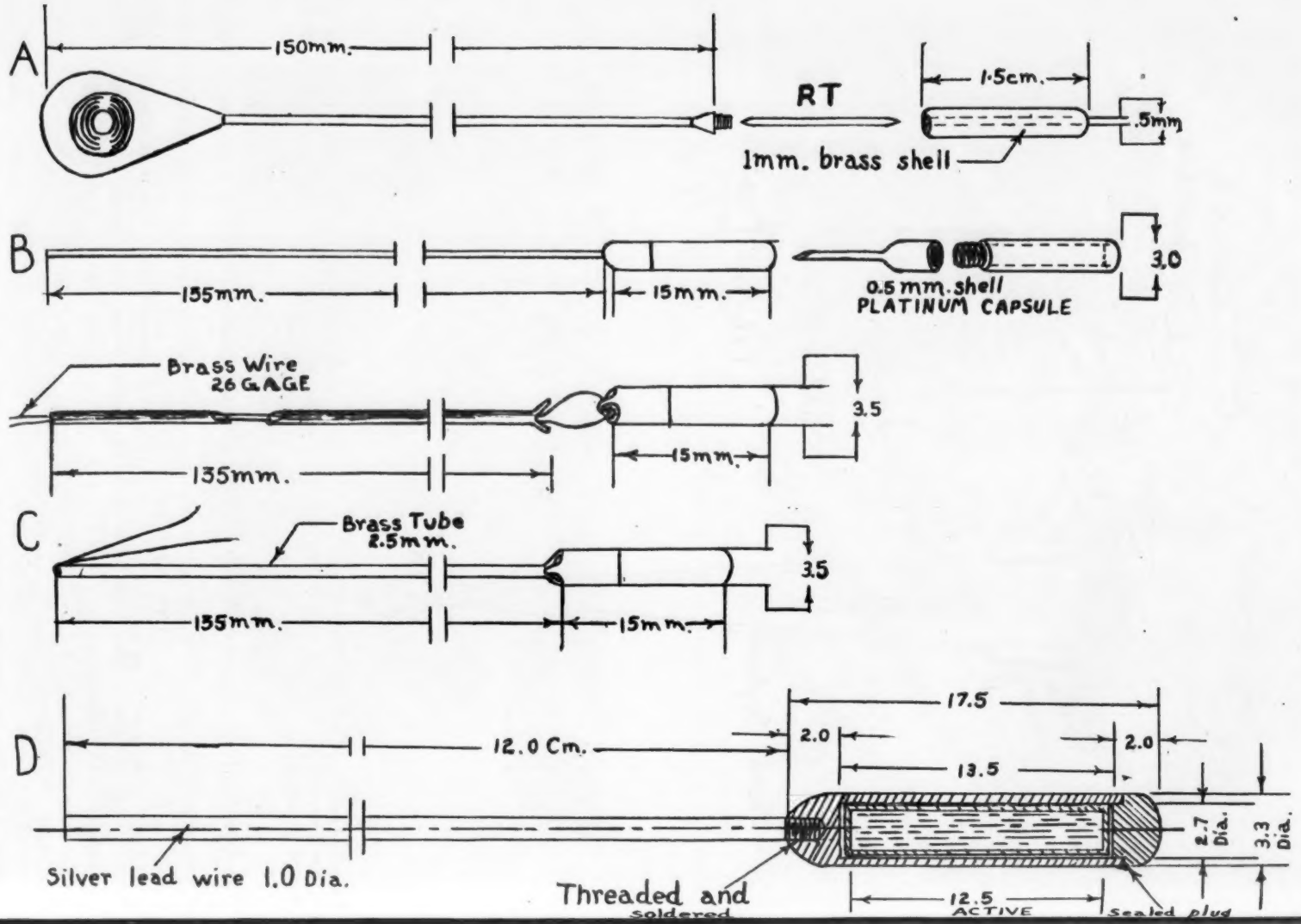
*Doses in Roentgens for 50 Mg. of Radium at Various Depths for Commonly Used Filters and Dosage Times (Compare Figure 9).**

Filter	Type of Radiation	1 Mm. Depth in Tissue			1 Cm. Depth in Tissue			2 Cm. Depth in Tissue			3 Cm. Depth in Tissue,
		6⅔ Min. = 5.6 Mg. Hr.	40 Min. = 33 Mg. Hr.	60 Min. = 50 Mg. Hr.	6⅔ Min.	40 Min.	60 Min.	6⅔ Min.	40 Min.	60 Min.	60 Min.
mm. platinum....	Pure gamma	....	1,500	2,250	..	265	400	..	70	100	45
m. brass.....	8% beta	....	1,800	.....	..	300	...	..	70	100	45
mm. monel metal	75% beta	1,520†	.....	.....	55	...	...	15	..	...	..

* The values in this table are computed for capsules 3 mm. in diameter and 1.5 mm. in active length. For a 0.3 mm. el metal capsule which is 1.5 cm. in active length and 2.3 mm. in diameter the doses are essentially the same as those listed. hange of active length from 1.5 mm. to 1.25 mm. will also make a negligible change in dosage. Platinum 0.65 mm. thick not reduce the dose as much as 5 per cent from that obtained with platinum 0.5 mm. thick.

† An exposure of eight and one half minutes equals 1,950 r, one of ten minutes 2,300 r and one of twelve and one-half utes 2,860 r at 1 mm. depth.

The table was prepared by Dr. Edith Quimby of the department of radiology of Columbia Presbyterian Medical Center.


A
150mm.
RT
1.5cm.
.5mm
1mm. brass shell
B
155mm.
15mm.
3.0
0.5 mm. shell
PLATINUM CAPSULE
Brass Wire
26 GAGE
3.5
135mm.
15mm.
C
Brass Tube
2.5mm.
3.5
135mm.
15mm.
D
12.0 Cm.
17.5
2.0
2.0
13.5
2.7 Dia.
3.3 Dia.
Silver lead wire 1.0 Dia.
Threaded and
soldered
12.5
ACTIVE
Sealed plug

EXPLANATION OF FIGURE 9

Applicators used for irradiation of the eustachian tube. *A*, Crowe type with a counterweight and a 1 mm. brass shell for use with radon. Eight per cent of the radiation from this capsule is beta radiation. Up to 1,000 millicuries can be held in the glass radon tube (*RT*).

B, platinum type, which filters out all beta radiation. Two of these are used at one time. Omission of the counterweight makes it more comfortable in the nose and makes it easier to slip rubber tubing over the end. (See fig. 8.)

C, adaption of a capsule designed for gynecologic work. Two of these, each containing 25 mg. of radium, work in the nasopharynx, but 50 mg. is better.

D, details of a capsule containing 50 mg. of radium in the double platinum shell used by me.

When filled with radium sulfate each contained 50 mg. of the radium salt.

The importance of the filtration has not been properly understood by some otologists doing this work. Dr. Samuel Crowe [2a] used 1 mm. of brass for 2 gram minutes (33 milligram hours) to each side, treating at four to six week intervals. One millimeter of brass filters out all but 8 per cent of the beta radiation.[13] On the other hand, the beta radiation may have comparatively more physiologic effect than the gamma radiation when it reaches the tissues concerned. In adults it is unusual to obtain the same results with a 0.5 mm. platinum filter as Crowe reported with brass unless four to six treatments are given. Crowe used a 1 mm. brass filter for only two or three treatments as a rule. With a platinum filter, if the dose is increased to 50 milligram hours to each side, the results are much more satisfactory than if 33 milligram hours is given, even though the interval between treatments is increased to four weeks instead of three weeks. Five-tenths millimeter of platinum filters out 100 per cent of the beta radiation.

Lately applicators containing 50 mg. of radium and having a filter of 0.3 mm. of Monel metal are being tried. These are used for six minutes and forty seconds (5.56 milligram hours) in contrast with the hour used by me with 0.5 mm. of platinum (50 milligram hours). If two applicators are identical except for filtration, the one with 0.3 mm. Monel metal delivers at a depth of 1 mm. in tissue seven times as much radiation as the one with 0.5 mm. of platinum, as determined by ionization measurements, according to Quimby.[14] Erythema tests with the same filter indicate a ratio of about eight times if calculated from the figures of Dean.[15]

It will be interesting to see whether the results with the mixed radiation from the Monel metal filter are as good as those with the radiation from brass or the pure gamma radiation provided by platinum. From physical measurements (table) it would seem that six minutes and forty seconds with 0.3 mm. of Monel metal is too short a time to obtain the same result as has been obtained with 50 mg. of radium in 1 mm. of brass for forty minutes or 0.5 mm. of

13. Glasser, O.; Quimby, E. H.; Taylor, L. S., and Weatherwax, J. L.: Physical Foundations of Radiology, New York, Paul B. Hoeber, Inc., 1944.

14. Quimby, E. H.: Personal communication to the author.

15. Dean, A. L., Jr.: Results of Skin Tests Made to Determine an Objective Dose for Radium Emanation, Am. J. Roentgenol. **10**:654 (Aug.) 1923.

platinum for one hour. Theoretically, to obtain 1,900 roentgens (r), as with brass, eight minutes would have to be used. To obtain the same result as with 0.5 mm. of platinum, eight and one-half minutes would have to be used. Since the potency of beta radiation is not as well understood as that of gamma radiation, increase in the dosage time in using Monel metal will have to be done with caution.

Since clinical observations and all the pathologic material available indicate that most of the lymphoid tissue that needs to be treated is on the surface of the nasopharynx (fig. 3), it would seem rational to use the Monel metal filter whenever possible. If this gives unsatisfactory results, it might be advisable to use supplementary roentgen ray therapy to attack the deeper parts of the eustachian tube.[1] The gamma radiation from a brass or a platinum capsule may be adequate to reduce the lymphocytic infiltration of the submucosal layers there (fig. 5).

It is possible that 1 mm. of brass is just the right filtration. It gives a relatively heavy dose on the surface, where autopsy material shows this to be most needed. It also gives a light dose peripherally in the eustachian tube, where smaller doses might be adequate. With 3 mm. of Monel metal as used there is again a heavy dose on the surface but practically none in the deeper tissues. (See figure 8 for the histologic structures reached at various depths and compare with the table for various filters and dosage times.) Doses of 100 r or less are effective on low grade inflammatory processes but have little direct effect on tissue.

Some years ago in the department of radiotherapy of the Presbyterian Hospital in New York, 63 patients were treated with roentgen ray therapy, 800 to 1,200 r [15a] being directed to each side through ports 5 cm. in diameter.[1] The treatments were directed so that the rays entered through the palate and different cutaneous areas on the cheek and the neck with each treatment. Results comparable to those obtained with radon and radium were obtained, but there were disadvantages in using roentgen ray. Flare-ups of otitis media were often observed with 150 or 200 r as used in another hospital. It was therefore thought unwise to give more than 100 r to each side at a sitting. This made it necessary for a patient to make several visits to the clinic during a period of three weeks. Even then there were a few slight reactions. In a [illegible] children mild otitis media developed with a [illegible] of only 100 r to each side, and a few had transi[illegible] parotitis. One woman, hypersensitive to ra[illegible] tion, showed erythema on the neck where [illegible] rays passed through the skin, after one tr[illegible] ment.

Several practical considerations are involv[illegible] in the selection of the type of radiation to [illegible] used. For example, if radium and radon are [illegible] available, there is no choice but to use high v[illegible] age roentgen therapy in spite of the fact tha[illegible] requires expensive and cumbersome equipm[illegible] is difficult to direct properly and requires [illegible] services of a radiotherapeutist for every tr[illegible] ment. The whole procedure is much simp[illegible] when two to four treatments are given w[illegible] radon or radium in juxtaposition to the tis[illegible] requiring irradiation.

If radium is available for other purposes [illegible] the containers are of suitable size, potency a[illegible] shape for use in the nasopharynx, it is abs[illegible] to obtain special radium applicators at gr[illegible] expense unless many patients are to be trea[illegible] over a long period. It is often easy to ad[illegible] capsules designed for other purposes and [illegible] insert them into the nasopharynx (fig. 9).[1] [illegible] radon is available, small groups of patients can [illegible] treated by appointment at no great initial e[illegible] pense. On the other hand, being able to tr[illegible] a patient at any time without a special shipm[illegible] of radon is more convenient. Whenever fun[illegible] are available to buy radium, special applicat[illegible] containing radium are preferable. Radium d[illegible] teriorates little in value, so that in the long r[illegible] the expense should, if anything, be less for [illegible] who do not have easy inexpensive access [illegible] radon. It is probable that both radium a[illegible] radon will be available in suitable applicators [illegible] a rental basis from various commercial hou[illegible] for those who only occasionally encounter p[illegible] tients needing this treatment.

There is said to be no danger if the tre[illegible] ment is properly done, but otologists a[illegible] advised to use radium and radon only in collab[illegible] ration with a competent radiotherapeutist. I[illegible] will be of greatest help in seeing that bo[illegible] patient and operator are properly protected a[illegible] if radon is used, will help in the inevitab[illegible] mathematics. If a proper type of applicator [illegible] used and the dosage is not tampered with, th[illegible] form of radiotherapy should be administered [illegible] the otologist, for only he can properly jud[illegible] the necessity for its use and the progress afte[illegible] ward.

15a. Measured in air—voltage, 1,108 kilovolts; amperage, 4 milliamperes; target skin distance, 16 cm.; filter, 3 mm. aluminum.

Most of those who have used radiation therapy improving the function of the eustachian tube enthusiastic about its efficacy. It is particu- y useful in airmen, for they rarely have ch underlying pathologic change. Shrinkage a little excess lymphoid tissue will often per- them to fly comfortably whereas previously y had had much difficulty. In addition to putting flyers back in the air, irradiation of the nasopharynx puts soldiers back in the firing line, civilians back to work, and children back in school. What is more, it forestalls the deafness which develops sooner or later from the recurrent attacks of otitis media, which are almost an inevitable sequel to malfunction of the eustachian tubes.

CLINICAL USE OF PENICILLIN IN INFECTIONS OF THE EARS, NOSE AND THROAT

COMMANDER AUSTIN T. SMITH (MC), U.S.N.R.

Penicillin became available for general clinical use in the United States Naval Hospital at Portsmouth, Va., in the fall of 1943. Its use in the treatment of infections of the ears, the nose and the throat was at first limited to severe infections which had failed to respond to treatment with sulfonamide compounds and other therapeutic measures and which were due to sensitive organisms. In the past few months, as the drug has become more available, it has been used in the average "run-of-the-mill" cases of such diseases as acute tonsillitis, acute maxillary sinusitis and acute or chronic otitis media. Consequently, this study comprises observations on approximately 100 cases, which can be divided into two groups—one representing some of the serious and difficult problems of therapy, and the other group, problems that are more ordinary but not always simple.

Penicillin is a specific agent, effective only against certain organisms, but since these organisms include the pyogenic cocci, which are most frequently responsible for the troublesome and serious infections in otolaryngologic practice, it is of particular value in this field. Because it is a specific agent and not a panacea, it is necessary to determine the bacterial nature of every infection against which it is used.

Conclusions as to the effectiveness of the drug have been reached in two ways: (1) by using as a control the previous course of the infection under other forms of treatment; (2) by witnessing results not seen in previous experience. For example, in some cases the customary surgical procedures were obviated entirely; in others the surgical treatment required was more limited and more conservative than usual. These methods of evaluation are practical and of unq tioned value, but they have their limitati The cases must be multiplied many times, the results repeatedly confirmed, to rule out possibility of chance.

A solution of the sodium salt was used in cases. It was given for the most part by in muscular injection. In some cases it was gi by intramuscular injection and local instillat and in others, (in cases of septicemia, for stance) it was started by the intravenous r and its administration continued, after a days, by the intramuscular route. In one of meningitis, intrathecal injection was c bined with intramuscular injection. The prim objective of any mode of administration is obtain an effective concentration of the drug the site of the infection for a sufficient length time for the substance to exert its maxim bacteriostatic action.

The minimal and the maximal effective d ages for various infections remain to be det mined. In each instance the type of organi and its susceptibility are an important factor the dosage. Hemolytic streptococci are e tremely susceptible, while staphylococci requ a considerably higher concentration. As t agent is carried by the blood stream, the a quacy of the blood supply and the ability the drug to come in contact with the organi are important considerations in deciding w the daily dose should be and the length of ti it should be given. In general, at this hosp it has been found that infections of soft tiss can be cleared by smaller doses, administe over a shorter period, than infections of bo cavities, such as sinuses and ears. As long the drug is not toxic, the policy, particula in regard to severe infections, should be: t much, too frequent, over too long a period rat than too little, too infrequent and over too br a period. It is advisable to check the pote of the penicillin being used from time to ti

As a statistical analysis of a small uncontrol series is of little value, I shall discuss the ca of each type of infection as a group, citi illustrative cases to bring out points of intere

From the Eye, Ear, Nose and Throat Department of the United States Naval Hospital, Portsmouth, Va.

Read before the Eastern Section of the American Laryngological, Rhinological and Otological Society at Philadelphia, Jan. 12, 1945.

This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the United States Navy. The opinions and views set forth are those of the writer and are not to be considered as reflecting the policies of the Navy Department.

CHRONIC SUPPURATIVE OTITIS MEDIA

The results of the treatment of chronic suppurative otitis media were disappointing in practically all cases. Penicillin was given intramuscularly in the dosage of 160,000 units per day for a period of two to three weeks. In some instances the ear became dry, but the time required did not point to any particular advantage over other methods of treatment. Three patients with marginal perforations in Shrapnell's membrane were treated by radical or modified radical mastoidectomy after three weeks of penicillin therapy. One could observe no effect on the pathologic condition of the mastoid process, which consisted of sclerotic, avascular bone interspersed with areas of necrosis. There was no apparent way in which the drug could be brought to the site of the infection other by local or by systemic administration.

ACUTE OTITIS MEDIA

In cases of acute otitis media with clinical and roentgen evidence of mastoiditis, the clinical response was prompt and often dramatic, and it was believed that the drug was an important factor in curing the infection and sparing the patient mastoidectomy. The time required varied from eight to twenty-one days. Only one patient with acute otitis media who received penicillin has been submitted to mastoidectomy. This was done because a second roentgenogram taken five days after beginning penicillin therapy was reported as showing increased destruction of bone. The clinical evidence of normal temperature, dry ear and decreased pain and tenderness indicated that the infection was subsiding, but it was thought advisable to explore the mastoid process. At operation there was no pus in the mastoid cells; they were filled with healthy granulations, and the appearance was that of a healing process. Culture of materials from the mastoid process gave negative results. The mastoid wound healed by primary union and without discharge. I believe that resolution and healing would have occurred without operation.

MASTOIDITIS WITH COMPLICATIONS REQUIRING MASTOIDECTOMY

Four patients who had mastoiditis with complications were treated with penicillin, this therapy being employed as an adjunct to mastoidectomy. One patient had petrositis; 1, meningitis and petrositis; 1, an extradural abscess, and 1, facial palsy. The hemolytic streptococcus was the active organism in all. All had received treatment with sulfonamide compounds for a period of two to six weeks without effect on the mastoiditis, or on the complications. It was felt that penicillin played an important part in the recovery of each. The operative wounds became clean and healed more rapidly than usual. In the case of meningitis and petrositis, the drug was probably life saving, but adequate surgical treatment was also necessary. After fourteen days' treatment consisting of mastoidectomy and intrathecal and intramuscular injection of penicillin and four additional days of intramuscular injection alone the spinal fluid became clear, the ear dried, the mastoid wound healed and the patient appeared to be on the road to recovery. Five days after penicillin therapy was discontinued severe headache in the left parietal region, nausea, vomiting, fever and double vision developed and there was a profuse discharge from the ear. Examination of the eyes revealed sixth nerve paralysis on the left side, and a roentgenogram showed evidence of petrositis. The mastoid process was reopened, and a suppurative tract was found extending into the posterior cells of the petrous pyramid. The spinal fluid remained clear. Cultures again showed hemolytic streptococci. The posterior cells were opened and drained, and penicillin was given again by intramuscular injection. The therapy was continued for eighteen days. By this time the mastoid wound had healed, the middle ear was dry and the patient seemed well; so it was discontinued. After seven days, headache, nausea, vomiting and purulent discharge from the ear recurred. The mastoid wound was opened to promote drainage, but no further exploration of the bone was done, and a third course of intramuscular injections of penicillin was given. In addition, the solution was instilled into the mastoid cavity through a small rubber tube drain. The penicillin therapy was continued for forty days, until all discharge from the mastoid wound had ceased, and culture of material taken from inside the rubber tube drain gave negative results. Hemolytic staphylococcus aureus was obtained from the wound and the mastoid process at this time.

We believe that the relapses in this case can be explained on the basis that infection was locked in cells of the petrous pyramid, that the area had been made relatively avascular by thrombosis and necrosis and that the infection could not be reached by the penicillin in sufficient concentration for it to be effective. This case illustrates the principle that evacuation of closed collections of pus is still necessary in spite of the efficacy of penicillin in controlling certain types of infection.

SINUSITIS

The cases of sinusitis studied represent acute and chronic infections of the frontal, the maxillary and the ethmoid sinuses, with and without complications and of varying degrees of severity. In all the cases cultures revealed organisms considered sensitive to penicillin.

The most notable results were obtained in patients suffering from acute multiple sinusitis, with involvement of the frontal, ethmoidal and maxillary sinuses on one side. Four of this group had orbital cellulitis or abscess. In all, it was felt that the drug was responsible for limiting the amount of surgical treatment that was necessary, or for eliminating it altogether. In regard to 1 patient, the first one treated with penicillin, it was considered imperative to drain the frontal sinus externally, as he appeared critically ill and threatened with intracranial complications. The infection was due to the hemolytic streptococcus, and he had received enough sulfadiazine to insure a high blood level, without any sign of improvement. At operation, the mucous membrane of the sinus was not disturbed except where the floor was removed for drainage, and the ostium, the nasofrontal duct and the middle meatus were not touched. The most notable feature of this case was the rapid reduction of swelling which occurred in the middle meatus within forty-eight hours, with reestablishment of drainage from the nasofrontal duct. Also, there was prompt reduction of the swelling of the mucous membrane of the frontal sinus at the outlet of the nasofrontal duct. Within three days a probe could be passed through the patulous nasofrontal duct into the frontal sinus. By the sixteenth day, healing had occurred, and all indications of infection in the frontal, ethmoid and maxillary sinuses had cleared.

With the other 3 patients no surgical drainage of the sinuses was done. In 1 patient an orbital abscess was incised and drained through a small incision below the eyebrow. In the other 2 the orbital cellulitis subsided without intervention. In all the rapid reduction of the swelling in the ethmoid cells, which was often polypoid in type, and the rapid establishment of normal drainage and ventilation through the middle meatus, were the striking features.

A patient with acute frontal sinusitis due to the hemolytic streptococcus showed marked improvement under sulfadiazine therapy and was apparently on the road to recovery when, in the fifth week, there suddenly developed marked swelling of his forehead, extending to the nose and both orbits. He had a high fever and was toxic. Roentgen study revealed thickening of the periostium and an area in the anterior part of the very deep right frontal sinus, which had the appearance of early osteomyelitis. Penicillin was given intramuscularly, and in nineteen days the swelling subsided, the osteomyelitis was arrested, and healed, and the frontal sinuses became clear. In this case a radical, deforming surgical procedure was averted and a dangerous frontal sinus infection cured. There seems to be little doubt that penicillin was the responsible factor.

In 1 case of chronic frontal sinusitis in which there was a mixed culture of Staph. aureus and Haemophilus influenzae, Staph. aureus was eliminated, but H. influenzae remained, and there was no clinical improvement. In another case of chronic sinusitis involving the right frontal, ethmoid and maxillary sinuses the infection, due to hemolytic Staph. aureus, was eradicated by a Caldwell-Luc operation, intranasal ethmoidectomy and administration of penicillin. The part that the drug plays in such cases is indeterminable, for in the past similar treatment without penicillin has been successful in many instances.

The effect of either the local instillation or the systemic administration of penicillin on maxillary sinusitis is difficult to evaluate. Many patients with acute sinusitis frequently get well under ordinary symptomatic therapy, or not at all, and the chronic infections often respond to ordinary local measures. In a small series it is impossible to rule out the possibility of chance. It is necessary to have a large series of cases, checked by an equal number of controls under the same circumstances, before definite facts as to the efficacy of penicillin over other types of therapy can be established.

The following is a summary of observations at this hospital on the treatment of maxillary sinusitis with penicillin:

A combination of systemic therapy and local instillation is better than either form of treatment alone. There is usually an associated infection of the ethmoid sinuses, particularly in cases of acute infection, and the systemic administration of penicillin has a marked effect on these sinuses, probably because of their better blood supply. This results in reduction of swelling in the middle meatus, with reestablishment of ventilation and drainage.

The infection is in the deep layers of the mucous membrane, and by local instillation penicillin cannot be kept in contact with all areas of the cavity long enough to allow it to penetrate to the deeper layer, in spite of its solubility.

the deep layers it must be carried by the stream. However, removing the pus from sinus by irrigation and then instilling 2 cc. penicillin solution (19,000 units of penicillin) tated contact of the drug with the infected es and seemed to hasten cure. In a few the infection was cleared up by irrigation local instillation alone. On the other hand, were a number in which infection that to clear up by local treatment responded the addition of systemic therapy.

INFECTIONS OF THE THROAT AND SOFT TISSUES

enicillin was of definite value in the treat- of acute follicular tonsillitis. The clinical nse was rapid, and it was necessary to ad- ster the drug only from five to seven days. hese cases administering the drug by intra- cular injection gave an advantage over medi- n by mouth, because of the painful swallow- particularly if there was peritonsillar inflam- ion present. Its rapidity of action and dom from toxicity make it a potent agent in treatment of this ordinary but frequently us disease. If given early, it should pre- the serious complications which not infre- ntly arise. However, it had no apparent ct on the course of rheumatic fever and ctious mononucleosis following acute tonsil- although the inflammation of the tonsils the pharynx subsided promptly.

n cases of cellulitis, carbuncles and furuncles limitation and resolution of the infection rred in a surprisingly short time. There marked improvement in the appearance of lesion within twenty-four hours, and recovery complete in five to eight days. Penicillin e therapy of choice for this type of infection. cases of furuncles or cellulitis of the nose and er eyelid it probably offers the best guarantee inst spread of the infection to the cavernous ses and intracranial structures.

Penicillin appeared to be an effective agent he treatment of Ludwig's angina. This has ays been a serious problem and is difficult reat. In 3 cases, all following tooth extrac- s, the condition cleared up in from five to days. In 1 instance through and through gical drainage was done; in the other 2 no gical procedure was necessary.

Two patients with bacteremia due to Staph. eus were successfully treated. In 1 patient bacteremia was a complication of cellulitis of back of the neck due to furuncles. Peni- n was not given until six days after the et of the infection of the neck when high fever developed and the patient became irrational and began expectorating blood-streaked sputum. A roentgenogram of the chest revealed evidence of small infarcts throughout both lungs. The temperature became normal on the eighth day of penicillin therapy; hemoptysis had subsided by the seventh day; the chest cleared and the systolic mitral murmur disappeared after the twelfth day. The patient received the drug for seventeen days—a total of 3,840,000 units. The value of penicillin in this instance cannot be questioned. Had it been given at the onset of the infection of the neck, I believe that the bacteremia would not have developed. Experience has shown it to be so rapid and effective in cases of cellulitis and furunculosis of staphylococcic or streptococcic origin that it should be the treatment of choice regardless of the apparent severity of the lesion. The small furuncle in a vascular area is always a potential source of bacteremia and fatal complications.

The second case of bacteremia illustrated the difficulty which arises from lack of definite information as to adequate dosage. The condition was due to hemolytic Staph. aureus and came as a complication of acute sore throat. Penicillin therapy was started at 120,000 units daily (15,000 units every three hours). The temperature continued to rise daily to 105 F., and toxemia was marked, although the pharyngitis and the cervical lymphadenitis subsided, until the seventh day, when the dosage was increased to 480,000 units a day. Within forty-eight hours the temperature dropped to normal, the toxemia disappeared, and the blood cultures became negative. The administration of penicillin was discontinued after six days of normal temperature. The patient appeared well, but there was a loud persistent systolic murmur over the pulmonic area. Four weeks later, sore throat again developed, the temperature rose to 103 F., and there were chills and marked toxemia. The blood culture was again positive for Staph, aureus. Penicillin therapy was started at 20,000 units every two hours. The temperature became normal and the blood sterile in five days. The administration of penicillin was continued for another week, and complete recovery resulted. I believe that the relapse would probably not have occurred had larger doses been given more frequently and treatment continued for a longer time after the original bout. Intensive, prolonged, uninterrupted treatment is indicated, especially in cases of serious staphylococcic infection, to eliminate the infection from hidden foci as well as from the blood stream.

In 2 cases of osteomyelitis of the mandible, penicillin appeared to be an aid in clearing up the infection, supplemental to surgical treatment of the bone. In both cases, however, it was administered over long periods, thirty-nine days and twenty-six days, and it is difficult to evaluate the efficacy of any therapeutic agent when it requires weeks or months rather than hours or days to obtain beneficial results. However, if used at the very onset of cellulitis and adenitis complicating the application of dental surgery, before involvement of bone occurs, it is effective. This was demonstrated in 3 cases, in 2 of which there was extensive involvement with abscesses of the parotid gland. One of the patients had received, in addition to surgical incision and drainage, roentgen therapy and treatment with sulfonamide compounds for thirty-six days. There was complete healing after eleven days of penicillin therapy with 120,000 units being given each day. All showed marked clinical improvement within two days and were completely well within two weeks. After osteomyelitis occurs, the infecting organism becomes sealed in and difficult to reach in areas of the bone made relatively avascular by thrombosis and necrosis, and surgical removal of the sequestrums is necessary.

SUMMARY

The results of the treatment of chronic suppurative otitis media were disappointing, and in cases that came to operation no effect on the pathologic condition of the mastoid process was noted.

In cases of acute otitis media, the clinical response was prompt and often dramatic, and the drug was an important factor in curing the infection and sparing the patient mastoidectomy.

In cases of mastoiditis with complica
requiring mastoidectomy, penicillin playe
important part in the recovery in each inst
and the operative wounds became clean
healed more rapidly than usual. In a ca
meningitis and petrositis, it was probably
saving, but adequate surgical treatment was
necessary in order to evacuate closed-in
lections of pus and permit the drug to reac
areas of infection in sufficient quantity t
effective.

Notable results were obtained by using p
cillin in cases of acute multiple sinusitis
and without complications and of varying de
of severity. It was responsible for limiting
amount of surgical work that was necessar
for eliminating it altogether. In cases of ch
sinusitis with mixed infection, local treat
and operative measures were necessary in a
tion to systemic treatment with penicillin,
the part that the drug plays in such cas
indeterminable; for in the past similar treatm
without penicillin has been successful in
instances. A combination of systemic ad
istration and local instillation of penicilli
better than either form of treatment alon
cases of maxillary sinusitis.

Penicillin was a potent agent in the treatm
of acute follicular tonsillitis but had no appa
effect on the course of rheumatic fever and
fectious mononucleosis following tonsillitis.

Penicillin was an effective agent in the tr
ment of Ludwig's angina and cellulitis or ade
complicating the application of dental surg
However, if osteomyelitis of the mandible
developed, it was necessary to supplement s
gical treatment with penicillin therapy, and
drug was administered over such a long pe
that it was difficult to evaluate its efficacy.

TRANSTUBAL INSTILLATION OF PENICILLIN IN ACUTE OTITIS MEDIA

COMMANDER JACOB A. WEISS (MC), U.S.N.R.

Many reports substantiate the therapeutic use of the local application as a supplement the administration of penicillin. It may be employed whenever the site of the suppurative process is accessible, as in the pleural, the peritoneal or the pericardial cavity, in joints, in wounds, fistulas, burns and compound fractures within the cerebral ventricles, the spinal canal, the nasal accessory sinuses or other preformed body spaces.[1]

A procedure for blowing penicillin into the tympanic cavity by the transtubal route will be presented in this report. It has been used in cases in which acute otitis media has not responded completely to the usual local measures and systemic treatment with either penicillin or one of the sulfonamide compounds. It has been found to be of value when the suppuration of the middle ear has reached a subacute stage of decreased but persistent drainage without necrosis in the mastoid process.

TECHNIC

The external auditory canal is wiped dry of secretion. The eustachian tube is then catheterized and inflated under compressed air pressure of 8 pounds to the square inch. An auscultation tube is used to note the passage of air. Any additional secretion thus expelled is wiped away. The tympanic membrane usually exhibits moderate inflammation and a small perforation. The patient's head is then tilted backward. With the catheter still engaged in the eustachian orifice, it is filled with a sterile isotonic solution of sodium chloride containing 1,500 units of the calcium salt of penicillin per cubic centimeter. Air pressure is applied, and the fluid in the catheter is blown into the tympanic cavity. Because some of the solution is dissipated along the course of the eustachian tube, it is necessary to refill the catheter and repeat the insufflation two or three times to insure that the penicillin enters the middle ear. The tip must be engaged firmly in the tubal orifice to prevent leakage into the pharynx. The no. 2 catheter used has a capacity of 0.5 cc. It is easily filled by using a small hypodermic syringe with a suitable needle. The passing of the penicillin solution into the middle ear is evidenced by a bubbling sound in the auscultation tube and by the appearance of a few droplets in the external auditory canal. The patient usually can distinguish between insufflation of air and that of fluid. There is little or no discomfort. The procedure is repeated daily until drainage ceases and the perforation closes.

REPORT OF CASES

CASE 1.—P. W. W., aged 22, was first seen because of acute otitis media of seventeen days' duration. In the ensuing ten days the suppuration ceased and the drum healed after intramuscular injection of 1,480,000 units of penicillin and oral administration of 50 Gm. of sulfadiazine. Roentgenograms of the mastoid process showed marked opacity with indefinite cellular detail. Five days after the patient left the hospital, the drainage recurred. Administration of 1,280,000 units of penicillin reduced the drainage to gelatinous mucoid secretion, which persisted. The white blood cell count and the temperature remained normal. The tympanic membrane showed moderate injection, absence of landmarks and a pinpoint central perforation. Transtubal insufflation of penicillin solution (1,500 units per cubic centimeter) on two successive days resulted in resolution of the tympanic inflammation and closure of the perforation.

CASE 2.—W. D., aged 19, presented acute otitis media of three days' duration with a profuse pulsating discharge, a temperature of 102 F. and a white blood cell count of 11,000. After an inadequate response to 70 grains (4.5 Gm.) of sulfadiazine in twelve days, penicillin was given over a period of thirteen days to a total of 1,860,000 units. The white blood cell count and the temperature declined to normal after five days. At this point, the twenty-eighth day of the otitis, the drum was dull gray, with a central perforation 1 mm. in diameter. Scanty seropurulent drainage continued for four days. Roentgenograms of the mastoid process revealed generalized haziness with no definite necrosis. However, there was no postauricular swelling or redness and no sag of the posterior-superior canal wall.

Transtubal insufflation of penicillin solution was done eight times in thirteen days. The aural drainage changed from seropurulent to mucoid and then ceased. Two days after the cessation of drainage the perforation closed. The inflammation of the drum cleared, and the landmarks reappeared. Hearing was 20/20 for spoken voice and 16/20 for whispered voice.

CASE 3.—In February 1945 R. C. J., aged 19, had scarlet fever. On February 20 acute otitis media developed as a complication. He received 1,070,000 units

---

This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the United States Navy. The opinions and views set forth are those of the writer and are not to be construed as reflecting the policies of the Navy Department.

1. (*a*) Lyons, C.: Penicillin Therapy of Surgical Infections in the U. S. Army, J. A. M. A. **123**:1007-1008 (Dec. 18) 1943. (*b*) Priest, W. S.: Penicillin Therapy, Am. J. Surg. **67**:280-295 (Feb.) 1945. (*c*) Florey, M. E., and Florey, H. W.: General and Local Administration of Penicillin, Lancet **1**:387-397 (March 27) 1943.

of penicillin from February 24 through March 2. Profuse aural drainage continued. On March 4 facial paralysis appeared. Mastoidectomy was performed on the same day, and extensive cellular necrosis was found. The postoperative course was uneventful. From March 5 through March 12 860,000 units of penicillin was given. Penicillin solution was instilled into the mastoid cavity. The postauricular incision was well healed by March 24, and the canal was dry. Drainage from the middle ear reappeared on April 2 and was persistent despite tubal insufflations and use of boric acid–alcohol solution and penicillin solution as ear drops. There was no drainage from the incision. On May 2 there was noted an increased amount of slightly odorous seropurulent secretion as well as notable injection of the drum.

Transtubal insufflation of penicillin solution (1,500 units per cubic centimeter) was done on May 3 and 4. The fluid came through into the external canal both times. On May 7 the inflammation of the drum had resolved, the landmarks reappeared and the drainage had ceased. The perforation closed on May 10 after one marginal application of trichloroacetic acid.

COMMENT

In acute otitis media penicillin has been used as drops in the external auditory canal with inconclusive results. In the presence of the customary thickened drum membrane with a small perforation it is doubtful whether the solution actually enters the middle ear.

In these cases the transtubal technic offers a method of applying the bacteriostatic drug to the site of infection. This follows the dictum of the Floreys[1c]: ". . . the problem of using penicillin locally is that of devising some means to apply a very soluble and diffusible substance so that a bacteriostatic concentration is constantly maintained. . . ." The catheteral route of penicillin insufflation should aid in the resolution of any inflammation present along the course of the eustachian tube as well as within the middle ear.

Swanson and Baker[2] have reported a technic of local penicillin treatment used in cases of chronic otitis media in which the drum membrane exhibited a large perforation and the middle ear was free from granulations or cholesteatoma. The solution is instilled into the external auditory canal and forced into the middle ear by means of a pneumatic otoscope. In a number of cases of this type I have instilled the solution of penicillin directly into the tympanic cavity, via the perforation, using an aural cannula. A preliminary irrigation is done with saturated solution of boric acid in 80 per cent alcohol to remove accumulated debris and pus. In these cases it is my impression that the response to treatment, as indicated by subsequent decrease or cessation of drainage, is more prompt than that following irrigations with boric acid–alcohol solution alone.

SUMMARY

In 2 cases of subacute otitis media and 1 case of postmastoidectomy drainage of the middle ear, penicillin solution (1,500 units to the cubic centimeter) was blown into the tympanic cavity by means of a eustachian catheter. This procedure appears to be of definite value as an adjunct to the usual systemic treatment. Further experience is necessary to evaluate the method.

United States Naval Construction Training Center, Davisville, R. I.

2. Swanson, C. A., and Baker, D. C., Jr.: The Use of Penicillin in Diseases of the Ear, J. A. M. A. 126: 616-620 (Nov. 4) 1944.

PENICILLIN IN OTOLARYNGOLOGIC PRACTICE

ISIDORE BERGER, M.D.
NEW YORK

Dr. Alexander Fleming's [1] interest in leukocytic and antiseptic action on bacteria during the period from 1914 to 1918 and his work on cultivations of staphylococcic colonies led to observations of bacterial lysis in areas of colonies of mold. He constantly sought information on bacterial inhibition and thus began his pursuit of this phenomenon. This particular mold belonged to the genus Penicillium and was identified as Penicillium notatum, the active substance which he called penicillin.

Garrod [2] described the extract of a mass culture of P. notatum as harmless to the mammalian body even though a thousand-fold the concentration necessary for therapeutic use was involved. Penicillin is unstable, and its salts of sodium and calcium are mainly in use. Its potency is expressed in terms of the Oxford unit, which is an arbitrary amount determined by a standard preparation, or the smallest amount of penicillin which when dissolved in 50 cc. of meat extract broth completely inhibits the growth of the test strain of Staphylococcus aureus. The purer penicillin is, the less is the toxicity. The latter is due mainly to impurities which cause a slight general reaction, such as lowering of the temperature and, locally, mild thrombophlebitis. The modus operandi of its bacteriostatic and bactericidal power is not clear. The process of bacterial division is perhaps inhibited, as suggested by Gardner's experiments.

The bacteriostatic and bactericidal properties of penicillin are active in blood and in pus, as well as in vitro. Concentration of penicillin does not make it antileukocytic, and it acts without regard to bacterial numbers, showing little or no toxicity for the tissues with which it comes in contact. Its action is not inhibited by broken-down products of inflammation. It has a selective action on specific species of bacteria, and the most sensitive are gram-positive, as staphylococci, pneumococci, streptococci and the gas gangrene group; in addition, the gram-negative group, the Neisseriae, including the gonococcus and the meningococcus, are sensitive. Penicillin-resistant organisms are the tubercle bacillus, the dysentery group, Proteus and Bacillus pyocyaneus (Pseudomonas aeruginosa). Penicillin is absorbed by the gastrointestinal tract, destroyed by the gastric juices and excreted rapidly in the urine. A certain blood level is therefore necessary, and continuous intravenous or intramuscular infusion must be maintained.

Florey,[3] in discussing the clinical use of penicillin, observed that the temperature may fall slowly, certainly not as quickly as with sulfanilamide therapy. In patients suffering from osteomyelitis, for instance, the temperature may often at first rise to a much higher level than before penicillin was used. She also observed that a roentgenogram of the diseased bone may show rapid absorption of tissue, pointing to the clearing up of the disease process and not to deterioration. It is necessary to make frequent bacterial examinations and the disappearance of organisms and the diminution of infection point to improvement. Penicillin has access to the infected area locally and systemically. If the bacterial flora does not disappear within about a week, resort to surgery may be necessary. In a case of infection with organisms that are penicillin-sensitive, the leukocytic count will show a drop, the red cells will show a rise, and locally there will be a reversal of the cardinal signs of inflammation and a return to normal function. After three to four weeks, surgical intervention is necessary if dead tissue or sequestrums remain and if bacteriologic evidence does not show subsidence of the infection.

Penicillin helps to prevent infection of wounds and may be used in sinal and aural infections. It promotes healing of burns and cutaneous grafts and is useful in sulfanilamide-resistant conditions.

Penicillin may be administered intravenously, intramuscularly, intrathecally and intracisternally,

From the Otolaryngology service of Dr. H. J. Burn, Harlem Hospital.

Read at the meeting of the Bronx Otolaryngological Society, Inc., in New York, Jan. 30, 1945.

1. Fleming, A.: Discovery of Penicillin, Brit. M. Bull. **2**:4-5, 1944.

2. Garrod, L. P.: Penicillin: Its Properties and Powers as a Therapeutic Agent, Brit. M. Bull. **2**:2-4, 1944.

3. Florey, M. E.: Clinical Uses of Penicillin, Brit. M. Bull. **2**:9-13, 1944.

as well as locally. Harris [4] uses continuous intramuscular infusion, which he finds saves time and avoids mild local reaction. Bordley and Crowe [5] suggested that penicillin be applied locally as a paste or a powder or that it be introduced by insufflation. Aspirating a wound and injecting penicillin by syringe also constitute a favorite local procedure. Since the presence of heavy metals and oxidation inhibit the action of penicillin, it is not advisable to use antiseptics or metallic preparations at the same time locally.

Keefer [6] advised that dosage depends on conditions, type of infection and other factors. In severe infections with hemolytic streptococci, Staph. aureus or pneumococci, with or without bacteremia, an initial dose of 15,000 to 20,000 units is given intravenously, with further dosage as follows: 5,000 units every hour by continuous intravenous injection of a solution of penicillin dissolved in isotonic solution of sodium chloride or a 5 per cent dextrose solution, the flow being regulated to deliver the desired dose per hour. He continues treatment, using smaller doses, for about a week after a normal temperature has been attained. In chronic infections an initial dose of 10,000 Oxford units is followed by 10,000 units every two hours, and local treatment as necessary. This schedule is revised to suit the clinical and the laboratory findings in the cases in question.

In Bloomfield's [7] opinion, some causes for penicillin failure are (1) failure to reach all parts of the wound, (2) bacterial resistence and (3) antecedent fibrosis preventing closure and healing. In cases of meningitis, intrathecal use is necessary, since penicillin does not pass freely from the blood to the cerebrospinal fluid.

Too brief treatment, too small doses, poor surgical drainage and overwhelming infection may also result in failure. Penicillin has not been found useful in combating infectious mononucleosis, mycosis fungoides or tuberculous paravertebral abscess.

Barker [8] reported on penicillin therapy in a case of Gradenigo's syndrome complicated by pneumococcic meningitis. The patient, a 35 old white woman, received, between Jan. 7 Jan. 13, 1943, 21 Gm. of sodium sulfadi and 65,000 units of penicillin, the latter i venously and intrathecally, following whic signs cleared, with smears and cultures o spinal fluid and the blood becoming neg although paralysis of the sixth and seventh n persisted.

Evans [9] published a report on the use of cillin in 2 cases of intracranial infection.

In the first case, the patient was admitted t hospital, Aug. 22, 1943, with a compound fractu the skull involving the left side of the frontal and the left cribriform plate. Cerebrospinal rhino appeared, followed by meningitis. After administr of 18.5 Gm. of sulfadiazine, Pneumococcus type 1 still present on smear and in a culture of the fluid, but following the administration of five doses of penicillin, a total of 2,085,000 units, the fluid was clear of bacteria.

In the second case, purulency was noted in the middle meatus with swelling and tenderness of the eye and the right side of the face. (Roentgeno did not show a fracture of the right frontal si Sulfadiazine was administered, without much imp ment. On June 24, 1943, weakness of the right of the face and of the whole left side of the body noted, and a diagnosis of abscess of the right fr lobe of the brain was made. Later, the abscess found to have ruptured into the right ventricle. September 15 another abscess formed. A craniot was performed, with evacuation of the abscess catheteral drainage, and 1,793,700 units of penic was administered through catheter locally, intrathec intramuscularly and intravenously. The patient discharged on November 20, and later examination vealed no neurologic findings or sequelae.

Bloomfield [10] described sinusitis caused Staph. aureus in a woman 32 years old, who been suffering from chronic frontal and maxill involvement for over four years and who finally cured with penicillin.

Four weeks prior to hospitalization the right ant was drained, and one week later she presented swel and tenderness over the right eye and the right of the face and the nose. A diagnosis of osteomye of the right maxilla was made. Culture of mate from the right maxillary sinus revealed Staph. au as the predominating organism. She received 2,690 units of penicillin between Sept. 25 and Oct. 31, 1 Necrotic sequestrums were removed from the r maxilla, following which the temperature dropped the draining sinus closed.

4. Harris, F. J.: Continuous Intramuscular Infusions of Penicillin, J. A. M. A. **126**:232 (Sept. 23) 1944.

5. Bordley, J. E.; Crowe, S. J.; Dolowitz, D. A., and Pickrell, K. L.: Local Use of Sulfonamides, Gramacidin (Tyrothricin) and Penicillin in Otolaryngology, Ann. Otol., Rhin. & Laryng. **51**:936-944 (Dec.) 1942; abstracted, Arch. Otolaryng. **38**:536-537 (Nov.) 1943.

6. Keefer, C. S., and others: Penicillin in the Treatment of Infections: A Report of Five Hundred Cases, J. A. M. A. **122**:1217-1224 (Aug. 28) 1943.

7. Bloomfield, A. L.; Kirby, W. M. M., and Armstrong, C. D.: A Study of "Penicillin Failures," J. A. M. A. **126**:685-691 (Nov. 11) 1944.

8. Barker, L. F.: Gradenigo Syndrome Complicated by Pneumococcic Meningitis: Recovery After Intensive Treatment with Penicillin and Sulfadiazi Am. J. M. Sc. **206**:701-703 (Dec.) 1943.

9. Evans, A. L.: Treatment of Intracranial In tions with Penicillin: Report of Three Cases, J. M. A. **124**:641-643 (March 4) 1944.

10. Bloomfield, A. L.; Rantz, L. A., and Kirby, M. M.: Clinical Use of Penicillin, J. A. M. A. **124**:6 633 (March 4) 1944 (case 7—sinusitis due to St aureus).

e case just described illustrates the neces- for prolonged treatment with large doses of cillin, and it also illustrates the effectiveness enicillin, since prior to its introduction or nistration such infections were fatal.

P., a woman aged 57, was admitted to Harlem ital, Nov. 5, 1943, because of a draining fistula e left maxilla of three weeks' duration, with a y of chronic disease of the left anterior and pos- groups of sinuses. The Wassermann test was ve, and roentgenograms showed marked clouding e left sinal group and, later, destruction of bone e left supraorbital area, the outer half of the left lla and the left zygoma. The organisms isolated the fistulous tract and the left antrum were ylococcus albus and streptococci.

e received antisyphilitic treatment and chemother- with no results. Penicillin was not obtainable June 16.

erations performed on this patient by Dr. H. J. an were as follows: incision and drainage of the ss over the left maxilla Nov. 2, 1943; the Caldwell- operation on the left side on Dec. 31, 1943; subse- ly, operation for osteomyelitis of the left half of rontal bone, at which time were removed the left of the frontal bone, the left zygoma and part of eft maxilla, the left infraorbital plate and part e left parietal bone, also part of the right half of rontal bone. At a still later revision the left er wing of the sphenoid bone was removed.

small draining tract developed on the right side e wound and persisted until a piece of the right of the frontal bone was removed, and with the nistration of 1,000,000 units of penicillin in the d from June 16 to June 23, 1944 prompt healing of ract followed. The patient was discharged for fur- medical observation, with a view to plastic recon- tion later.

Wickstrom and Hebble [11] reported the results enicillin therapy in a case of acute suppura- ethmoiditis with orbital abscess and sep- nia, following a nasal cold.

e patient, a man 20 years of age, was admitted to ospital on Oct. 20, 1943. Pus eroded the orbit, and al cellulitis developed, caused by Staph. aureus, pure ths of which were obtained by culture of the nasal arge, of material from the orbital abscess and of the . Swelling and tenderness developed over the left and the left eye, and there was edema of the scalp. The mucous membrane of the nose and the turbinates was congested, with pus discharging from the middle meatuses. The temperature was 105 F. Ocular motion was limited, and the patient was in a stuporous state. The white cell count was 26,000. Roentgen examination revealed a clear left frontal sinus and left maxillary sinus, but cloudy ethmoid cells on the left. The patient received 310 grains (20 Gm.) of sulfadiazine and blood transfusions, with no improvement. Word aphasia developed. The ocular fundi showed nothing abnormal. On October 22, penicillin treatment was begun. On October 25, convulsions were noted, as well as weakness of the right arm and leg. Incision with drainage of the left orbital abscess was performed, and Staph. aureus was found to be the predominating organism. Penicillin therapy was continued until November 5, with improvement total except for some slight ptosis of the left upper eyelid and slight limitation of motion of the eyeball.

Wolf [12] published an article on thrombosis of the cavernous sinus with hemolytic streptococcic bacteremia occuring in a boy aged 10. The focus of infection was a furuncle of the bridge of the nose. Multiple thrombosis developed in the lungs and the kidneys with hemolytic streptococcic bacteremia. Sixty-four grains (4.14 Gm.) of sulfadiazine and 500,000 units of penicillin were administered within a period of nineteen days. The blood level of sulfadiazine was 8 mg. or more per hundred cubic centimeters. In my opinion, sulfadiazine cleared up the bacteremia due to hemolytic streptococci, but penicillin cleared up the septicemia of staphylococcic origin of the original focus. Neither drug when used exclusively caused any change in the condition of the patient.

CONCLUSIONS

Penicillin is a powerful bactericidal and bacteriostatic agent surpassing the sulfonamide drugs in its power to combat certain infections and to promote the healing of wounds. It is to be used in sulfanilamide-resistant conditions. Much more extensive scientific research is necessary to reveal its further clinical applications.

888 Grand Concourse.

Wickstrom, O. W., and Hebble, H. M.: Acute urative Ethmoiditis with Orbital Abscess and icemia, Treated with Penicillin, U. S. Nav. M. Bull. 379-1380 (June) 1944.

12. Wolf, J. W.: Thrombosis of the Cavernous Sinus with Hemolytic Streptococcus Bacteremia: Treatment by Intravenous Injection of Sulfadiazine and Penicillin, with Recovery, Arch. Otolaryng. **40**:33-37 (July) 1944.

LARYNGEAL NEUROSIS INCIDENT TO MILITARY SERVICE

CAPTAIN BENJAMIN RISEMAN
AND
LIEUTENANT COLONEL WALTER J. AAGESEN
MEDICAL CORPS, ARMY OF THE UNITED STATES

The laryngeal neurosis is that symptom complex in which the laryngeal complaints of the patient are not attributable to organic disease but to some form of emotional conflict. That this type of neurosis is a definite clinical entity has been demonstrated by Jackson,[1] Greene,[2] Berendes[3] and others.

The chief complaint of the 17 patients under our observation was prolonged hoarseness of rather sudden onset. Aphonia and diplophonia were rare occurrences. Sensory disturbances, such as paresthesia and hyperesthesia, were not encountered. Only one of the patients had experienced combat duty, all others having been stationed continuously within the continental limits of the United States since their induction or enlistment.

A complete clinical study was made in all cases to rule out organic disease of the larynx. Direct laryngoscopy, including the use of the anterior commissure scope or a tracheoscope, with thorough exploration of every part of the larynx and the subglottic region, was performed in every case. Malingering, infection in the nose, throat and larynx, vocal abuse, excessive use of alcohol or tobacco and climatic conditions were all excluded as possible etiologic factors.

Ten of the patients presented the typical picture of dysphonia plicae ventricularis,[1] or vicarious phonation[4]; i. e., voice was produced with the ventricular bands or false cords instead of the true vocal cords. In these cases on phonation the ventricular bands were markedly hyperactive and approximated in the midline just before the true cords. Restraint of the ventricular bands with the forceps during direct laryngoscopy evoked an excellent sound on phonation of the true cords, demonstrating clearly the normal function of the latter. The remaining of the patients revealed excellent approximation of the vocal cords at the instant of phonation but as the phonatory effort continued, the vocal cords assumed various shapes. In 2 patients the vocal cords bowed upward, leaving a narrow crescentic glottic chink, with consequent loss of the expiratory blast. In another patient, the anterior one third of each true cord became rigid on phonation and presented an oval chink in the region of the anterior commissure. As phonation continued, however, the cords would again approximate each other. In 2 patients this type of closure and tension was found to involve the posterior one third of each vocal cord, simulating paralysis of the interarytenoid muscles. In another patient no laryngeal abnormality could be detected.

After investigation to rule out organic disease the soldiers were studied by physicians in the neuropsychiatric service. In each case, mental or emotional[6] conflict was found to be the etiologic basis of the hoarseness. Accordingly, therapy was directed toward helping the patient to solve his or her individual problem, or to adjust to the situation, so far as was feasible within the regulations of the military service. The results of this therapy were generally excellent. With patients, however, the usual otolaryngologic and neuropsychiatric therapy failed, and other procedures were used which produced a prompt cure. It is our opinion that such measures are not justified except in the occasional case in which all other forms of therapy have failed. Fifteen of the patients were returned to duty. On completion of therapy normal function of the larynx and an excellent voice were regained. In some instances, voice recordings taken before and after therapy helped to impress the soldier with the true nature of his condition. The patient

Presented before the New England Oto-Laryngological Society, in Boston, November 15, 1944.

1. Jackson, C., and Jackson, C. L.: Diseases and Injuries of the Larynx, New York, The Macmillan Company, 1942.

2. Greene, J. S.: Psychiatric Therapy for Dysphonia; Aphonia; Psychophonasthenia; Falsetto, Arch. Otolaryng. **28**:213-221 (Aug.) 1938.

3. Berendes, J.: Ztschr. f. Hals-, Nasen- u. Ohrenh. **44**:78-84, 1938.

4. Tucker, G.: J. Laryng. & Otol. **51**:563-573 (Sept.) 1936.

5. Winkelman, N. W.: M. Clin. North Am. **21**:1211-1220 (July) 1937.

6. Greene, J. S.: J. Nerv. & Ment. Dis. **95**:299 (March) 1942.

harged from the military service were enlisted nen with numerous somatic complaints, of ch hoarseness was but one. Even with r many complaints, therapy had restored their es to normal before their discharge from the ice.

From the brief summaries of the cases, which to follow, it will be noted that each patient a mental or an emotional conflict arising n frustration of his or her desires. The ngeal manifestations represented an escape n a problem for which the patient could find other solution.[6] This is one form of physio- c interpretation of a psychosomatic disorder. nature of the mental or emotional conflict t be ascertained, and therapy directed toward dissolution. The approach is of necessity vidual, although in many cases definite pat- s seemed evident as therapy was applied. up therapy was tried, but its results were stionable.

The following types of therapy, either singly in combination, were applied: (1) sugges- ,[7] (2) suggestion under narcosis,[8] (3) reas- ance,[1] (4) relaxation,[9] (5) taking advantage the patient's credulity, (6) appealing to the riotism of the patient, (7) taking the patient ware in an unguarded moment, (8) speech cation [10] and (9) local treatment of a harm- nature.

SUMMARIES OF CASES

Case 1.—A soldier 25 years old complained of sudden rseness with periods of aphonia for two months prior admission. Direct laryngoscopy revealed bowing of posterior third of each vocal cord on phonation. patient admitted great anxiety concerning parental roval of his recent step in marrying one not of his gion. Under narcosis induced with sodium amytal talked normally. While he was under narcosis, the gestion was made that his voice would improve. s, coupled with a letter to his parents and the re- ion of parental approval of the marriage, brought ut gradual disappearance of the hoarseness.

Case 2.—A soldier aged 40 complained of hoarseness ive months' duration. He stated that at a previous ion when he was investigated for pharyngitis he told that he had a cancer of the larynx. His rseness developed immediately afterward. Exami- ion revealed dysphonia plicae ventricularis. Con- ued reassurance that thorough examination had re- led no evidence of cancer produced gradual clearing the hoarseness.

Case 3.—A soldier 29 years old complained of hoarseness which developed on the day of his induction into the army, two weeks prior to his admission to this hospital. Direct and indirect laryngeal examination revealed bowing and laxness of both true vocal cords with each phonatory effort. The emotional factor was found to be a fear that his wife and parents would suffer privations, since he was their sole support. The procurement of jobs for his wife and his father brought about rapid disappearance of his hoarseness.

Case 4.—A soldier 28 years old had complained of recurrent hoarseness over a period of nineteen months. Direct and indirect laryngeal examination revealed dysphonia plicae ventricularis, the background for which was found to be a fear of asphyxia. The hoarseness dated from the time that four other soldiers and himself were overcome by gas inside a tent in Mississippi. The others all died, the patient being the sole survivor following artificial resuscitation. Neuropsychiatric and otolaryngologic therapy were unsuccessful. After direct laryngoscopy, the soldier was told that a large tumor had been removed from his larynx, and he was shown a specimen borrowed from the pathologic laboratory. There was immediate return of the normal voice.

Case 5.—A soldier aged 29 complained of hoarseness with a tendency toward aphonia and diplophonia of four months' duration. These symptoms appeared suddenly on awakening one morning. Direct and indirect examination revealed dysphonia plicae ventricularis. He was found to be extremely anxious about his aged mother who, he stated, was at home without proper care. Suggestion, relaxation and speech education were tried without success. All other therapeutic efforts failed. The use of alcohol was discussed with him, and one night shortly afterward he became markedly intoxicated. On awakening he talked with a normal voice, which has remained for two years without further use of alcoholic beverages.

Case 6.—A 27 year old soldier complained of aphonia which developed only when he wished to yell. His conversational voice was normal. No pathologic abnormality of the larynx was found. This patient had been in the army for more than two years and had been a truck driver during the entire period. Two months prior to his hospitalization he had been told by his commanding officer that he was to be promoted to sergeant. The soldier feared to assume the added responsibility. After advising his commanding officer that we considered this patient to be poor leader material, the commanding officer agreed to waive the patient's promotion. After the patient was informed of the action taken, it was found that he could yell without losing his voice.

Case 7.—An enlisted woman 28 years old complained that for a period of three months she had been unable to talk in a conversational voice. Direct laryngoscopy revealed dysphonia plicae ventricularis. The background was found to be resentment directed at her superior officers. She was taken unaware in an unguarded moment by a question requiring a prompt yes or no answer. Her answer was a sudden return of normal voice. Because of numerous associated somatic complaints, she was discharged from the military service as having severe psychoneurosis.

Case 8.—A 23 year old soldier complained of sudden hoarseness while in school taking a course in engineering. Examination revealed dysphonia plicae ventricularis. He was found to be fearful of not passing the

7. Jackson and Jackson.[1] Winkelman.[5] Greene.[6]

8. Clerf, L. H., and Braceland, F. J.: Ann. Otol., in. & Laryng. **51**:905-916 (Dec.) 1942.

9. Tarrasch, H.: Clinical Aspects of Functional arseness, Arch. Otolaryng. **36**:53-70 (July) 1942.

10. Froeschels, E.: Hygiene of Voice, Arch. Otoyng. **38**:122-130 (Aug.) 1943.

course in engineering. Reassurance and speech education brought about gradual disappearance of the hoarseness.

CASE 9.—A soldier aged 33 complained of hoarseness of five weeks' duration. Direct laryngoscopy revealed dysphonia plicae ventricularis. He was found to be fearful of overseas duty. Reassurance and appeals to his patriotism evoked a fairly rapid disappearance of the hoarseness.

CASE 10.—A 22 year old soldier complained of a dry throat for one week followed by hoarseness of ninety-four days' duration. Examination revealed dysphonia plicae ventricularis. This patient had been on duty on an island outpost with only one furlough in over two years. Communication with his commanding officer to obtain his transfer to a new station brought about rapid cessation of his hoarseness.

CASE 11.—A soldier aged 38 complained of hoarseness of three months' duration which developed while he was in the hospital with arthritis of the lumbar part of the spinal column. Examination revealed upward bowing and laxness of both vocal cords on phonation. The background was found to be a fear of cancer. This fear developed after the patient had read an article on the subject in a current periodical. Reassurance and repeated spraying of the larynx with saline solution brought about gradual return of the normal voice.

CASE 12.—A soldier 27 years old complained of hoarseness of three weeks' duration, which developed shortly after he recovered from pneumonia. Examination revealed dysphonia plicae ventricularis. This patient was worried about the support of his parents inasmuch as his two other brothers were being inducted into the military service. Reassurance brought about gradual disappearance of the hoarseness.

CASE 13.—A soldier aged 29 complained of hoarseness on awakening one morning. The condition persisted for two months. Direct laryngoscopy revealed dysphonia plicae ventricularis. He was found to be fearful of overseas duty. Many types of treatment were tried without improvement. This patient was able to use his voice except when he was around officers or ward personnel. In an unguarded moment he was heard to use his voice by the nurses and the ward master. This resulted in immediate disappearance of his hoarseness.

CASE 14.—A 27 year old army nurse complained for a period of two weeks of hoarseness, recurrent loss of the spoken voice and a tendency of the voice to crack. Examination revealed dysphonia plicae ventricularis. The emotional factor was fear of overseas duty. All methods of treatment failed. The patient was disqualified for overseas duty because of severe dysmenorrhea. This resulted in gradual improve of her voice.

CASE 15.—A 25 year old soldier complained of ho ness of four months' duration following a twelve hike. Examination revealed upward bowing of vocal cords, with consequent lack of tension on ph tion. The soldier feared to assume responsibility. assurance and repeated suggestions that he had exce qualities of leadership brought about gradual disap ance of his hoarseness.

CASE 16.—A captain in the chaplains' corps, 32 y old, complained of hoarseness which developed w he was stationed in New Caledonia in June 1943. stated that it was more of an inability to force voice or speak loudly. Direct laryngoscopy reve mild redness of both true cords with lack of ten of the posterior third of each cord just after the be ning of the phonatory effort. It was interesting note that his first speech difficulty arose not long a the explosion of a naval ammunition dump on the isl The neuropsychiatric service made a diagnosis of p choneurosis, conversion hysteria. Reassurance tha would be assigned to duty in this country near his h and suggestion therapy brought a slow return of nor intensity to his voice.

CASE 17.—An enlisted woman aged 22 develo sudden hoarseness to the point of whispering. She seen in consultation. Direct laryngoscopy reve dysphonia plicae ventricularis. The underlying ca was found to be resentment of the fact that she going to be discharged from the service on a C.D. A diagnosis of psychoneurosis, mixed type, modera was made by the neuropsychiatric service. Her v returned spontaneously within twenty-four hours. cause of numerous other somatic complaints, she had be discharged from the service.

CONCLUSIONS

1. Laryngeal neurosis exists as a defini clinical entity.

2. Mental or emotional conflicts are the eti logic basis of the voice changes.

3. The clinical laryngeal findings are not co stant, the most frequent finding being dysphon plicae ventricularis.

4. Therapy consists chiefly of dissolution the the individual's basic mental conflict.

5. A high percentage of patients can be r turned to full military duty after proper therap

Lovell General Hospital, Fort Devens, Mass.

EVALUATION OF THE LEMPERT FENESTRA NOV-OVALIS OPERATION IN THE TREATMENT OF OTOSCLEROSIS

REPORT ON THIRTY-SIX PATIENTS WHO WERE SELECTED FOR THIS OPERATION

SAMUEL D. GREENFIELD, M.D.
BROOKLYN

It will no doubt be left for later decades to aim the Lempert fenestra nov-ovalis operation the outstanding surgical achievement in dern otologic surgery. Not since the advent he simple mastoidectomy of Schwartze and adical operation of Staacke has anything so mentous been evolved in the field of otology. a boon to humanity it certainly ranks in imtance with these two surgical procedures.

There is little wonder indeed that otologists inally greeted this work with so little enthusi- and so little credulity. To begin with, they always been concerned primarily with the dication of disease of the temporal bone. No gress had ever been made surgically in the oration of hearing. Then, in addition, knowlof the pathologic involvement in otosclerowith its progressive characteristics, precluded feasibility of employing surgical measures in effort to retard its progress, let alone the sibility of restoring that which was already

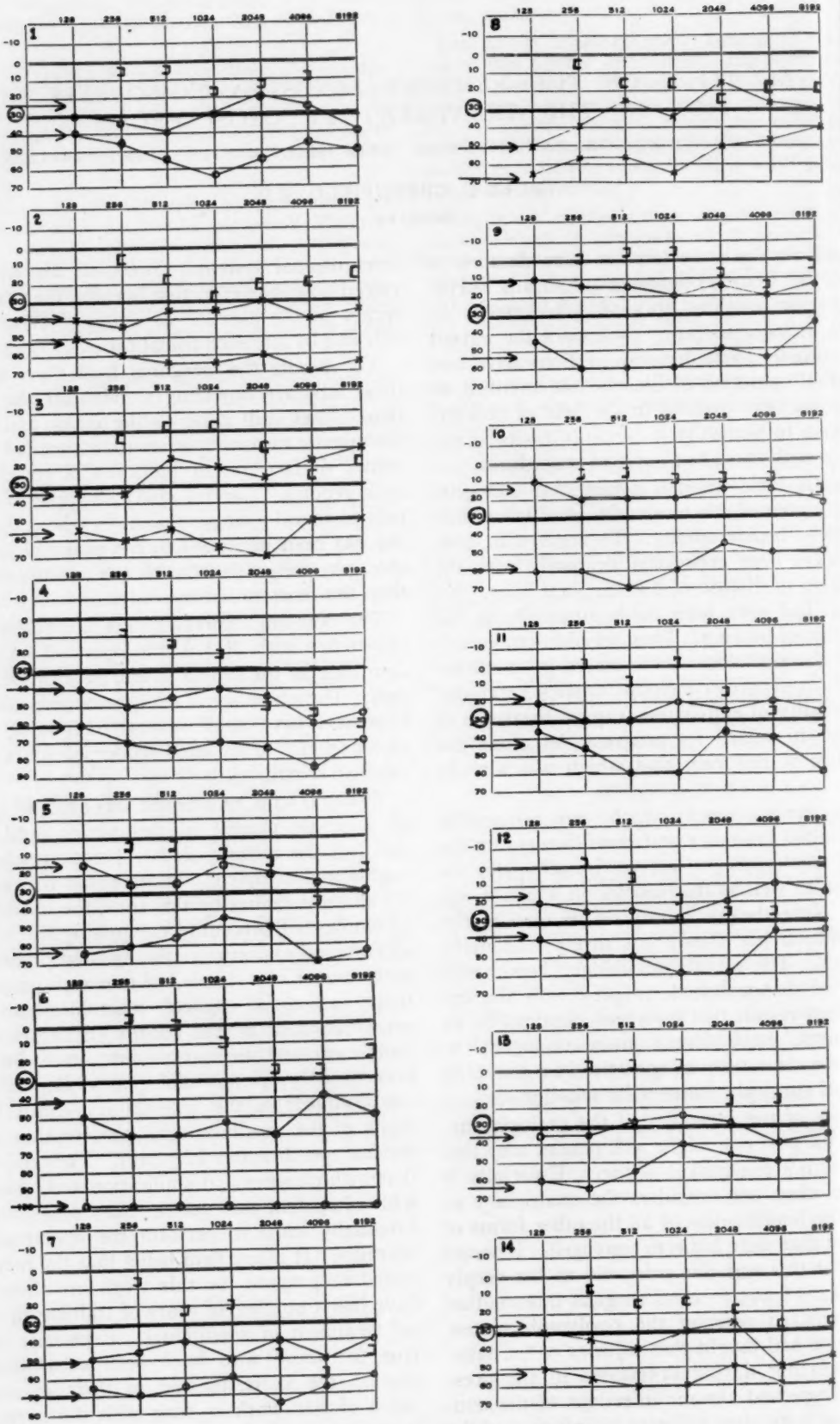
t was these concepts which were responsible the initial hesitancy and unwillingness on the of otologists to accept immediately the ration as well as the theories on which it was ed. Nevertheless, purely on its own merits operation has slowly but surely won many ocates. Its sound physiologic basis, now futably demonstrated, coupled with the exordinary results that have been obtained by its loyment, have forced most otologists to pt the fenestration operation as the only redited surgical treatment for otosclerosis.

n view of the ingenuity of the otologic sur- in the past one might well ponder why this rk was not undertaken sooner. Especially is true when one considers the inadequacy as l as the hopelessness of all the other forms of tment that were hitherto employed. It seems me that this was due primarily to the deeply ted fear of any form of surgical intervention ich required opening the perilymph spaces. perience had taught that injuries of the labyth occurring during operations in the pres- of acute and chronic infections of the temral bone were often followed by infection of the cerebrospinal system. Otologists are well convinced now, however, that opening the perilymph spaces in the absence of acute infection is not followed by any such complications.

Yet despite the foregoing facts there are still those who are unwilling to advocate the operation. They still cling to the many and varied therapeutic measures other than surgical. As a matter of fact, recent literature is replete with such reports. Careful study of these, however, fails to reveal a single patient in whom the hearing has been improved to the practical, serviceable, physiologic level with any treatment other than the fenestration operation.

The opinions expressed here are based on an experience with 36 patients operated on by me according to the technic acquired with Dr. Lempert. The series is not a large one; nevertheless, from it I have made several interesting observations which to my mind render it a more or less valuable contribution.

To begin with, no attempt was made to operate on a single patient in this series until every detail of the technic of the operation was thoroughly and completely mastered on the cadaver. As all must realize by this time, the operation is a complicated procedure comprising the steps of an endaural exposure of the mastoid process, the performance of a simple but thorough mastoidectomy, a partial radical mastoidectomy with preservation of all the minute structures in the middle ear and the epitympanic space, the creation of a tympanomeatal plastic flap and the establishment of the fenestra nov-ovalis in the dome of the vestibule with preservation of the delicate membranous labyrinth. I am convinced that with patience and application and, above all, with competent instruction many otologists will eventually learn to perform the operation successfully. It is my firm belief that the men best suited to prepare for this work are those who have had a number of years of training in surgical treatment of mastoiditis. Especially is this true for those who have been accustomed to employ the curet technic in their operations. Most of this work is done with the curet, and it takes quite a while for one to become adept



(See legends on opposite page)

skilled in its use. As Marvin Jones so aptly it:

> his is an operation that cannot be bluffed. Those ors who do not possess the natural surgical ability ich is necessary to perform this operation, even ugh they may have good training, will not get the results. Only those doctors who have ability and willing to spend months . . . yes, even years, ecting the technique under competent instruction, ld attempt this most difficult surgical procedure.

It has been a sad mistake on the part of e men who have attempted the operation hout heeding the foregoing advice. As a lt there are dead labyrinths and facial paraly-. Not only have these patients been un-tunate victims, but these failures have been ruitful source of condemnation for the opera-n itself.

There is no doubt that the improvement of ring in the properly selected patient will be ctly proportional to the skill of the operator. who do this work must agree that this is an disputed fact. Since success of the opera-n depends on the careful and exact execution the various steps of the operation, it follows essarily that the more meticulous one becomes regard to the minutest details, the better are results. It is for this reason that one finds that the subsequent groups of patients operated on by the same surgeon show an increasing percentage of successful results.

The most controversial phase of the whole subject at the present time is the question of the indication for the operation. In this series I have not limited myself alone to operating on the patients whose symptoms clinically were those of otosclerosis but have included patients with other forms of conductive deafness. Although it is difficult to make a positive diagnosis of otosclerosis without a histologic examination, nevertheless, one is justified in making such a diagnosis in a patient who presents the following findings: (1) a family history of deafness; (2) audiometric evidence of conductive impairment; (3) absence of any history of previous otitic infection; (4) rapid loss of hearing following pregnancy; (5) normal drum membranes; (6) patent eustachian tubes. I would differentiate this group from those in whom audiometric studies reveal a conductive type of deafness but who have a previous history of otitic suppuration, as evidenced by a drum membrane that is dull or thickened or presents scarring with healed perforations and secondary membranes. However, in the selection of patients for operation the determination of the cause of the conductive deafness is not so essential. What

---

EXPLANATION OF FIGURES 1 TO 14

Fig. 1.—Audiogram for the right ear of Mrs. B. D., d 28, operated on Dec. 11, 1941. In this and all sequent audiograms the numbers at the top represent ible vibrations (tonal frequencies); those at the left, ibels. Normal hearing is represented by the zero el. Hearing for bone-conducted tones is indicated brackets (right ear]; left ear [). Hearing for air-ducted tones is shown in the curves (right ear, les; left ear, crosses).
In this audiogram the lower arrow indicates the pre-rative threshold of hearing for air-conducted tones; upper arrow, the postoperative threshold.

Fig. 2.—Audiogram for the left ear of Mr. C. F., d 34, operated on Dec. 29, 1941. The lower arrow icates the preoperative threshold of hearing; the er arrow, the postoperative threshold.

Fig. 2.—Audiogram for the left ear of Mrs. S. S., d 30, operated on Feb. 1, 1944. The lower arrow icates the preoperative, the upper arrow the post-rative, threshold of hearing.

Fig. 4.—Audiogram for the right ear of Miss M. B., d 29, operated on Feb. 15, 1942. The lower arrow icates the preoperative threshold of hearing; the er arrow, the postoperative threshold.

Fig. 5.—Audiogram for the right ear of Miss S. B., d 27, operated on May 12, 1942. The lower arrow icates the preoperative threshold of hearing; the er arrow, the postoperative threshold.

Fig. 6.—Audiogram for the right ear of Mrs. E. F., d 21, operated on June 19, 1942. This patient ered a typical loss of hearing after the operation; upper arrow indicates the preoperative threshold of ring and the lower arrow the postoperative threshold.

Fig. 7.—Audiogram for the right ear of Miss A. E., aged 22, operated on June 26, 1942. The lower arrow indicates the preoperative threshold of hearing; the upper arrow, the postoperative threshold.

Fig. 8.—Audiogram for the left ear of Mrs. E. B., aged 30, operated on July 6, 1942. The lower arrow indicates the preoperative threshold of hearing; the upper arrow, the postoperative threshold.

Fig. 9.—Audiogram for the right ear of Mrs. S. L., aged 33, operated on Oct. 6, 1942. The lower arrow indicates the preoperative, the upper arrow the post-operative, threshold of hearing.

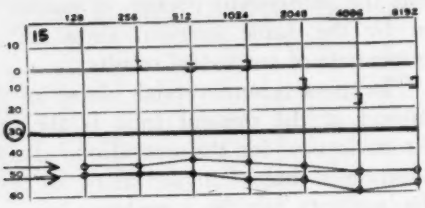
Fig. 10.—Audiogram for the right ear of Miss S. K., aged 33, operated on Oct. 14, 1942. The lower arrow indicates the preoperative threshold of hearing; the upper, the postoperative threshold.

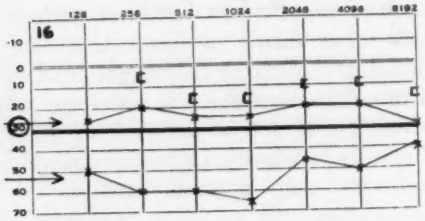
Fig. 11.—Audiogram for the right ear of Miss S. F., aged 25, operated on Nov. 10, 1942. The lower arrow indicates the preoperative and the upper arrow the post-operative threshold of hearing.

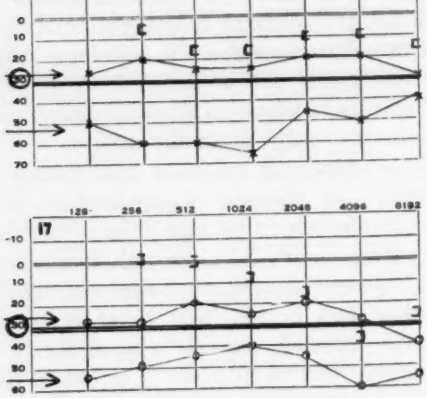
Fig. 12.—Audiogram for the right ear of Mrs. B. K., aged 39, operated on Feb. 4, 1943. The lower arrow indicates the preoperative threshold of hearing; the upper arrow, the postoperative threshold.

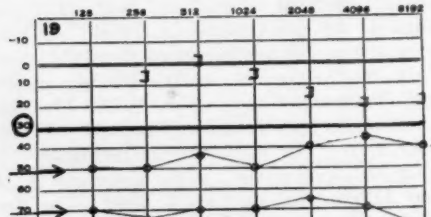
Fig. 13.—Audiogram for the right ear of Mrs. E. S., aged 47, operated on July 6, 1943. The lower arrow indicates the preoperative threshold of hearing; the upper arrow, the postoperative threshold.

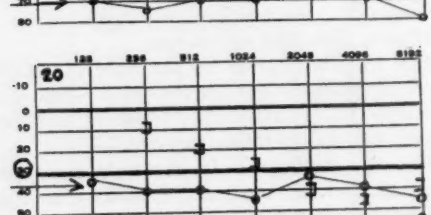
Fig. 14.—Audiogram for the left ear of Mrs. W. W., aged 27, operated on Sept. 12, 1943. The lower arrow indicates the preoperative threshold of hearing; the upper arrow, the postoperative threshold.

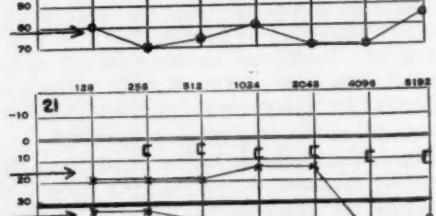


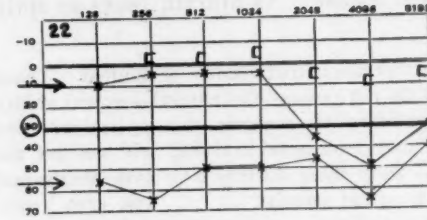


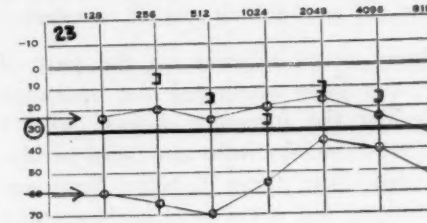


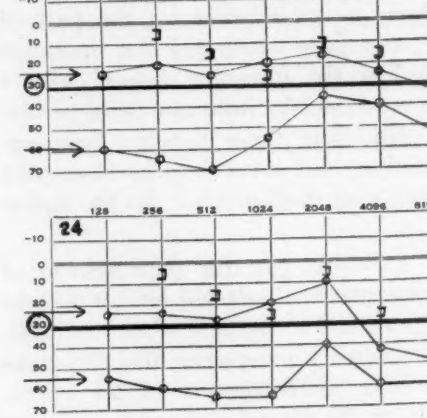


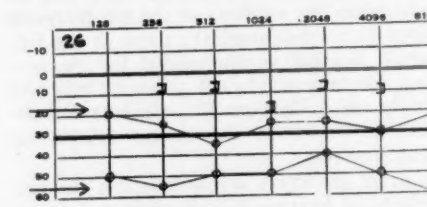


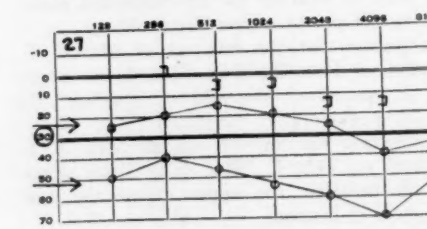


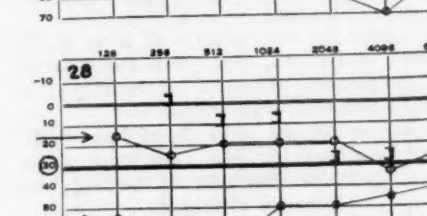












(See legends on opposite page)

of prime importance is the extent to which deafness has or has not progressed to involve auditory nerve.

The patients who are ideally suited for operation and in whom one can expect the maximum surance of success are those in whom the nerve completely free from involvement. Accord- to the principles originally set down by mpert, operation is indicated in those patients whom the bone conduction for tones of 512, 24 and 2048 double vibrations indicates ade- ate cochlear function. The closer the bone nduction curve approaches the normal, the tter is the prognosis. At the present time I lieve that this is the safer rule to follow.

In the selection of patients for operation I ose, for the most part, only those patients in om the threshold of hearing for bone-con- cted tones of 512, 1024 and 2048 double rations was at or above the 30 decibel level. leviated from this rule in regard to 4 patients: s. 4, 7, 18 and 20 in the series. In all of these tients the threshold for bone-conducted tones 512 and 1024 double vibrations was within rmal limits but that for 2048 double vibrations s well below the 30 decibel level. This would nd to indicate nerve involvement. It will be ted in the audiograms of these 4 patients that spite the fact that I obtained an improvement hearing in all of them, and in some a gain of much as 25 to 30 decibels was registered, nevertheless I failed to raise their hearing to the practical, serviceable level. It appears, therefore, that from my own personal experience these patients were not the most suitable for operation. At least to my mind, one should not expect the results obtained in the patients with purely conductive types of deafness.

On the other hand, Lempert, who is constantly experimenting in an effort to establish a more consistent and scientific basis for operation, has deliberately operated on a number of patients with frank nerve deafness. For some reason or other he has obtained good results in about 20 per cent of these. What the explanation for this can be is problematic. It certainly points to the fact that the various methods available today for testing patients are not altogether satisfactory. On the other hand, it may be that the interpretations or the deductions from these findings are incorrect. It seems that occasionally both the audiometer and the tuning forks are inadequate and therefore fail to disclose the degree of residual nerve function. However, until newer and better methods are devised, it will be the better policy to follow Lempert's original dictums.

The ages of the 36 patients operated on by me ranged from 17 to 51. There were 34 females and 2 males. The first patient was operated on three years, and the latest patient two months, prior to the time of writing.

EXPLANATION OF FIGURES 15 TO 28

Fig. 15.—Audiogram for the right ear of Mrs. R. C., ed 28, operated on Sept. 23, 1943. The lower arrow dicates the preoperative threshold of hearing; the per arrow, the postoperative threshold. This patient's sult was not satisfactory.

Fig. 16.—Audiogram for the left ear of Mrs. L. W., ed 33, operated on Sept. 27, 1943. The lower arrow dicates the preoperative and the upper arrow the stoperative threshold.

Fig. 17.—Audiogram for the right ear of Mrs. F. B., erated on Nov. 3, 1943. The lower arrow indicates e preoperative threshold of hearing; the upper arrow, e postoperative threshold.

Fig. 18.—Audiogram for the right ear of Miss A. S., ed 29, operated on Dec. 16, 1943. The lower arrow dicates the preoperative, the upper arrow the post- erative, threshold of hearing.

Fig. 19.—Audiogram for the right ear of Miss A. S., ed 35, operated on Dec. 23, 1943. This patient's aring loss was increased after the operation. The per arrow indicates the preoperative threshold of aring; the lower arrow, the postoperative threshold.

Fig. 20.—Audiogram for the right ear of Mrs. M. S., ed 32, operated on Jan. 17, 1944. The lower arrow dicates the preoperative and the upper arrow the post- erative threshold of hearing.

Fig. 21.—Audiogram for the left ear of Mrs. D. A., ed 30, operated on Jan. 23, 1943. The lower arrow dicates the preoperative threshold of hearing; the pper arrow, the postoperative threshold.

Fig. 22.—Audiogram for the left ear of Miss L. B., aged 17, operated on March 22, 1944. The lower arrow indicates the preoperative threshold of hearing; the upper arrow, the postoperative threshold.

Fig. 23.—Audiogram for the right ear of Mrs. E. A., operated on March 29, 1944. The lower arrow indicates the preoperative, the upper arrow the postoperative, threshold of hearing.

Fig. 24.—Audiogram for the right ear of Miss A. D., aged 25. The lower arrow indicates the preoperative and the upper arrow the postoperative threshold of hearing.

Fig. 25.—Audiogram for the right ear of Mrs. F. O., aged 51, operated on May 15, 1944. The lower arrow indicates the preoperative, the upper arrow the post- operative, threshold of hearing.

Fig. 26.—Audiogram for the right ear of Mrs. B. H., aged 44, operated on May 12, 1944. The lower arrow indicates the preoperative, the upper arrow the post- operative, threshold of hearing.

Fig. 27.—Audiogram for the right ear of Mrs. V. S., aged 34, operated on May 17, 1944. The lower arrow indicates the preoperative, the upper arrow the post- operative, threshold of hearing.

Fig. 28.—Audiogram for the right ear of Mrs. H. K., aged 48, operated on June 6, 1944. The lower arrow indicates the preoperative threshold of hearing; the upper arrow, the postoperative threshold.

In an analysis of the state of hearing of these patients I am reporting only on those who were operated on prior to six months before writing. My reason for not including any of the later ones is of course obvious. Sufficient time has not yet elapsed to evaluate the results in those patients.

There were 28 patients operated on prior to six months before writing. Of these 21 have had their hearing restored to the practical, serviceable, physiologic level. In other words, the hearing for speech tones has been brought up within the 30 decibel range. Fifteen of these patients hear 512, 1024 and 2048 double vibrations at or above the 30 decibel level; 4 hear two of these tones at this height, and 2 hear one of these tones at this mark. All of these 21 patients can carry on their usual occupations without any difficulty, can associate with their friends without any embarrassment and can attend all forms of entertainment without requiring artificial hearing devices.

Of the remaining 7 patients, 4 were the ones previously alluded to as having had beginning nerve involvement. In all 4 of them the threshold of hearing for bone-conducted tones of 2048 double vibrations was well below the 30 decibel level. In all of them hearing was improved but in none of them was I successful in bringing it up to the practical level. However, all but 1 of them are greatly appreciative of the improvement they did obtain.

In the remaining 3 patients the results were totally unsuccessful. One of them had practically no improvement in hearing following the operation. One had a further loss in hearing. One lost the hearing entirely. The audiograms of these 3 patients are shown respectively in figures 15, 19 and 6.

An analysis of the data on these patients definitely reveals the etiologic factors that were responsible for the failures in 2 of them. In the third instance I can only speculate as to the cause. Patient 15 is the one in whom no satisfactory etiologic factor could be found. This patient had an uneventful operation and postoperative course. The operative cavity was completely healed and dry within three months. At no time after the operation did the hearing ever come above the preoperative level. The patient was apparently ideally suited for operation, according to the audiometric and tuning fork standards. The only explanation I can offer for the failure of the hearing to improve is a closure of the round window. There is, however, no preoperative test at present by which one can determine whether this condition is present.

Patient 19, in whom the hearing became w after operation, had the usual postoperative r tion. On about the fourth day all the symp of labyrinthine irritation had subsided. On seventh postoperative day a full dressing performed. The paraffin plug was remove the usual way. Soon after the dressing patient began to experience vertigo. She bec nauseated and vomited, and the nystagmus turned. These symptoms continued for weeks and then gradually subsided. The finally healed, but audiometric examinati revealed a loss of hearing beyond that wh she had prior to operation. There is no d that in this patient labyrinthitis developed the first full dressing. What could have pre tated this infection after a period of appa quiescence can be deduced only from the that at the dressing the tympanomeatal flap disturbed. As a rule, by the eighth day the has firmly adhered to the underlying bone. is possible to conceive, however, that blood lecting under the flap sometime after opera can delay the healing process. In this removal of the paraffin plug may detach tympanomeatal flap and expose the labyrinth infection. I believe this is what took place in patient and that it was responsible for destro most of the function of the labyrinth. The fist test elicited a positive reaction in this patient.

Patient 6 lost the hearing completely. Dur the final stages of the operation, when endosteum was being removed over the ve bule, a small spicule of bone perforated ampullated end of the membranous horizo semicircular canal. This was followed by ac suppurative labyrinthitis. It ran the us course and resulted in complete loss of b auditory and vestibular functions in that ear.

CONCLUSIONS

1. The Lempert fenestra nov-ovalis operati is the only form of treatment for the restorati of serviceable, practical hearing in patients w otosclerosis.

2. No man should attempt the operation unl he has spent sufficient time studying and p paring himself for this work under compet instruction.

3. The operation is a safe procedure in t hands of those especially trained to do t operation.

4. The patients most suitable for operation a those suffering with the purely conductive ty of deafness without any evidence of ner involvement.

169 New York Avenue.

SSUE CHANGES PRODUCED IN THE NASAL MUCOUS MEMBRANE OF ORMAL MICE BY PROLONGED LOCAL ADMINISTRATION OF SOME SOLUTIONS CONTAINING SULFONAMIDE COMPOUNDS

F. T. CALLOMON, M.D.
WITH THE TECHNICAL ASSISTANCE OF LORAINE G. LINTON
PHILADELPHIA

Numerous reports in the literature[1] reveal erences of opinion regarding human toler- e of the solutions of sulfonamide compounds d in local treatment of the nasal mucous mbrane. Recently, as a result of investiga- s of the physiologic range of the hydrogen ion centration of the secretions of normal nasal ues in situ (p_H fluctuating between 5.5 and) and of the changes in it observed in the rse of nasal and sinus diease of man, Fabri- t[2] proposed a new basis for the selection of l remedies to be administered intranasally. stressed that markedly alkaline preparations ally exert an irritating effect on the nasal ue, impairing the ciliary function and dam- g the lfactory lining. The therapeutic prob- has been to develop "a nontoxic medica- , compatible with ciliary action," of the same drogen ion concentration as the nasal tissue d therefore "non-traumatizing to the mucous mbrane." Furthermore, this author has stated t under adequate conditions of observation g solutions with a p_H range of 5.5 to 6.5 do appear to affect markedly the nasal hydrogen concentration, and since the sodium salts sulfonamide compounds are usually highly aline (with p_H ranging between 10 and 11), their solutions are by no means free of unfavorable caustic reactions.[2b] Fabricant concluded that, contrary to the generally accepted idea, "it is now time to acidify the nasal mucosa, not to alkalize."

To prevent the irritating effect associated with high alkalinity of solutions of sulfonamide compounds, Yonkman[3] and his associates and Blackford[4] recommended the use of propylene glycol as a menstruum for sulfathiazole and its sodium salt as well as for other sulfonamide compounds. They found, in particular, that 3 per cent solutions of sulfathiazole in propylene glycol were well tolerated because of the slight acidity of those solutions, with p_H values within the physiologic range of the nasal p_H of man. Propylene glycol also seemed to have the effect of maintaining stable solutions.

Recently the importance of animal experimentation as a basis for testing the local effect on nasal tissues of preparations containing sulfonamide compounds has been emphasized.[5] Such studies permit the observer to note at convenient intervals the development of injury on groups of animals during and following prolonged local administration of drugs. Fabricant[1a] has summarized the experimental results obtained to date. In such experiments, Futch, Rosenvold and Stewart,[5a] also Gundrum,[1c] used rabbits, while Hunnicutt[5b,c] used mice. Clinical trial of new drugs recommended for nasal use

From the Research Institute of Cutaneous Medicine; John A. Kolmer, director.

1. (*a*) Fabricant, N. D.: The Local Use of Sulfonides in Nasal and Sinus Infection: An Analytic view, Am. J. M. Sc. **206**:546, 1943. (*b*) Freund, M.: Local Use of Some of the Newer Sulfonamide lutions in Diseases of the Ear, Nose and Throat, e, Ear, Nose & Throat Monthly **23**:104, 1944. Gundrum, L. K.: Effect of the Newer Sulfanilamide rivatives on the Nasal Mucosa of Rabbits, Arch. olaryng. **37**:209 (Feb.) 1943; in discussion on Hunutt,[5c] p. 64. (*d*) Kully, B. M.: The Use and Abuse Nasal Vasoconstrictor Medications, J. A. M. A. 7:307 (Feb. 10) 1945.

2. Fabricant, N. D.: (*a*) Significance of the p_H of sal Secretions in Situ, Arch. Otolaryng. **34**:150 uly); 297 (Aug.) 1941; (*b*) Nasal Medication: A actical Guide, Baltimore, Williams & Wilkins Comy, 1942; (*c*) Clinical Significance of the p_H of Superial Mucous Membranes of the Head, Eye, Ear, Nose Throat Monthly **23**:219, 1944; (*d*) footnote 1 *a*.

3. Yonkman, F. F.; Craver, B. N.; Lehman, A. J., and Chase, H. F.: Propylene Glycol as a Menstruum for Sodium Sulfathiazole, J. A. M. A. **118**:1317 (April 11) 1942.

4. Blackford, R. W.: Propylene Glycol a Menstruum for Sulfathiazole, Laryngoscope **53**:164, 1943.

5. (*a*) Futch, C. E.; Rosenvold, L. K., and Stewart, C. E., Jr.: Caustic Effect of Sodium Sulfathiazole Solution on Nasal Mucous Membranes, J. A. M. A. **119**:7 (May 2) 1942. (*b*) Hunnicutt, L. G.: Reaction of Mucous Membranes to Five Percent Solution of Sodium Sulfathiazole, Arch. Otolaryng. **36**:837 (Dec.) 1942; (*c*) The Effect of Drugs on the Nasal Mucous Membrane, Tr. Pacific Coast Oto-Ophth. Soc. **26**:53, 1941. (*d*) Gundrum.[1c]

should be postponed until adequate laboratory and animal experimentation justify their use.

Of course, there are great anatomic differences between the nasal organs of small laboratory animals and those of man and, consequently, different conditions for the spread and concentration of locally administered drops of chemical solutions. However, since we were concerned only with the study of the local effect of solutions of certain sulfonamide compounds of various p_H values on the nasal mucosa, we confined our study to microscopic examinations of tissue specimens of laboratory animals. The results observed with the various solutions and the various concentrations which we administered were correlated with the respective p_H values. Only mice were used in our experiments.

SOLUTION USED IN OUR EXPERIMENTS

The solutions which we used included: (*a*) Three per cent sulfathiazole solution in propylene glycol, according to the suggestion of Yonkman and his associates[1b]; the freshly prepared solution showed a p_H value of 5.1.

(*b*) Pure propylene glycol having a p_H of 5.4.

(*c*) Various solutions prepared from two newer sulfonamide drugs not yet tested for nasal use—the diaminodiphenyl sulfone derivative diasone, whose high bacteriostatic efficacy has been demonstrated by Raiziss[6] and whose beneficial effect on experimental tuberculosis has been indicated,[7] and succinylsulfapyrazine, recently found to be at least equal to sulfaguanidine in its bacteriostatic effect on the intestinal (coliform) flora of normal mice.[8] Both the diasone and the succinylsulfapyrazine solutions were of two different concentrations; i. e., they contained 2 per cent and 3 per cent of the drug. The 2 per cent and 3 per cent concentrations of diasone were prepared in propylene glycol and the 3 per cent concentration in distilled water as well; the 2 per cent and 3 per cent concentrations of succinylsulfapyrazine were prepared only in propylene glycol. To keep the solutions stable for the duration of our experiments, we added 10 per cent sodium bicarbonate to the 3 per cent diasone solutions and 0.45 per cent sodium bicarbonate to the 2 per cent succinyl sulfapyrazine solution.[9] For the 3 per cent solution of the latter compound the sodium salt of succinylsulfapyrazine was used. All our solutions were kept in amber bottles. They remained stable for the duration of our experiments except for the 2 per cent solution of diasone in propylene gl... This solution, to which no sodium bicarbonate ... added, had to be eliminated from further experiment... after sixteen days, when decomposition became evi... The 2 per cent diasone solution had a lower p_H t... any other preparation, i. e., 4.8. The 3 per cent ... tions of diasone and of sodium succinylsulfapyra... had p_H values of 8.3, 8.8 and 8.1, while the p_H of 2 ... cent succinylsulfapyrazine in propylene glycol wa... the physiologic range.

(*d*) We also included one of the many commer... products which are combinations of a vasoconstri... and a sulfonamide drug. As Kully[1d] reported recen... one or another sulfonamide compound has been ad... to almost every type of vasoconstrictor. Sulfathia... in particular, has appeared in at least thirty such c... binations. The commercial product which we used w... an aqueous solution of sodium sulfathiazole and deso... ephedrine, with a p_H value of 9.2.

(*e*) As a control series, a group of mice was gi... isotonic solution of sodium chloride. Believing t... the saline solution used, with its p_H value of 7.2, w... not harm the nasal mucosa, we felt that any cha... from normal observed subsequently would reflect ... sole effect of the daily manipulation in administeri... the solutions.

EXPERIMENTAL PROCEDURE

Sixty-nine mice of 20 to 25 Gm. weight were u... The animals were kept in individual cages and u... formly fed pulverized Purina dog chow.[10] Vari... groups of mice were treated with the different prepar... tions, instilled on the nasal mucous membrane twice ... day for fourteen days, as follows:

- 9 mice with 3 per cent sulfathiazole in propylene ... glycol
- 6 mice with pure propylene glycol
- 6 mice with 2 per cent diasone in propylene glyc...
- 9 mice with 3 per cent diasone in propylene glycol ... which 10 per cent sodium bicarbonate had be... added
- 9 mice with 3 per cent diasone in aqueous solution ... which 10 per cent sodium bicarbonate had be... added
- 6 mice with 2 per cent succinyl sulfapyrazine in pro... pylene glycol to which 0.45 per cent sodium bica... bonate had been added
- 9 mice with 3 per cent sodium succinyl sulfapyrazi... in propylene glycol
- 9 mice with a commercial solution containing desox... ephedrine and sodium sulfathiazole in aqueous sol... tion
- 4 mice with isotonic solution of sodium chloride

In addition, 2 untreated mice of the same stock serv... for demonstration of the histologic structure of the na... tissues of normal mice kept under equal conditions ... care and feed.

One third of the mice of each sulfonamide compou... group and a half of those making up the saline soluti...

6. Raiziss, G. W.: Diasone: A New and Active Chemotherapeutic Agent, Science **98**:350, 1943.

7. Callomon, F. T.: New Derivatives of Diamino-Diphenylsulfone, Am. Rev. Tuberc. **47**:97, 1943.

8. Callomon, F. T., and Raiziss, G. W.: Effect of Oral Administration of Succinyl Sulfapyrazine on Bacterial (Coliform) Flora of the Intestine of Normal Mice, J. Pharmacol. & Exper. Therap. **79**:200, 1943.

9. We do not wish to pass any judgment on the stability of our solutions over a longer period than that of the experimental part of our study, i. e., about five to six weeks. The p_H values were determined and the prepared drug solutions supplied by Dr. G. W. Raiziss, of the Dermatological Research Laboratories Division of Abbott Laboratories, North Chicago, Ill.

10. Purina dog chow contains, according to t... Ralston Purina Company, St. Louis, the following i... gredients: meat meal, dried skim milk, a vitamin ... (riboflavin) concentrate, carotene, cod liver oil, brewe... dried yeast, wheat germ, corn grits, wheat cereal, co... cereal, dried beet pulp, molasses, steamed bone me... iodized salt.

up were killed after five days of treatment; another
d and the remaining half of the saline solution
up were killed on the morning following the
rteenth day of treatment; the remaining third of each
onamide compound group was killed on the fifth
after cessation of treatment. Autopsies were made
particular attention to the possible presence of
nchopneumonia. Transverse sections of the noses
e prepared exhibiting the nasal cavities at both sides
he septum; the specimens selected for microscopic
stigation were decalcified and sections stained with
atoxylin-eosin.

ur technic was based on Hunnicutt's procedure.[5b, c]
o ear speculums of different gage were cut in two,
larger parts being used. At opposite sides, close
he rim, the speculums were perforated to fix two
on threads long enough to hold the speculum after
head of the mouse was put into the larger end.
ding the animal with one's left hand and the metal
culum by means of the two threads with the fourth
ifth fingers of the same hand, one will easily keep
mouth of the mouse closed. Therefore, only nasal
iration will occur during treatment. Capillary
ts were used to place one drop of the solution
each of the nostrils, thus covering the nasal open-
s. The mouse head being tipped back, as Hunnicutt
gested, the drops will be sucked into the nasal cavi-
after a few seconds. Any overdose in adminis-
ing the drops may change the conditions of the
eriment so that the chemical will be aspirated into
respiratory organs and cause bronchial pneumonia.
ing the procedure correctly, one can conduct the
erimental work without assistance.

In a preliminary experiment 2 mice were treated as
cribed by Hunnicutt [5b] with a solution of methylene
e and autopsies were performed three and six
onds, respectively, after two drops of the solu-
n had been placed on the nostrils. In the first mouse
staining of the surface of the nasal cavities was
ost complete, while in the second mouse it was com-
te as far as the trachea.

MACROSCOPIC OBSERVATIONS

During the period of treatment all the animals
re normal in appearance, in motility and in
ir intake of food. Their response to the trauma
treatment was restricted to a few minutes'
ction of amotility or excitement, shaking the
d or scratching of the nose.

Autopsies.—At the end of treatment, the nasal
cous membrane of the mice revealed either no
croscopic change or marked symptoms of
itation, such as edema or hyperemia, with or
thout some amount of purulent exudate, and
a few cases a small slough adherent to the
cous membrane of the septum. This slough
s blood stained in 1 mouse given the 2 per cent
sone solution for fourteen days. Broncho-
eumonia was found in 2 mice of the sulfa-
azole–propylene glycol group and in 1 mouse
ven 2 per cent succinylsulfapyrazine drops.
ese 3 animals, in the order stated, died on the
rd, seventh and twelfth days of treatment.

MICROSCOPIC OBSERVATIONS

The true extent of injury was determined by microscopic examination. The pathologic changes observed in the nasal tissues consisted of: (*a*) slight to considerable inflammation of the mucous membrane; (*b*) focal or extensive disorganization or destruction of the olfactory epithelium, with or without excess of the mucus covering its surface, sometimes associated with focal damage of the ciliary part of the mucosa; (*c*) small or considerable amounts of purulent exudate in the nasal cavities, sometimes in the sinuses also. Generally these tissue changes, when observed, persisted through the period of treatment, but showed less, or returned to normal, on the fifth day after discontinuance of treatment.

Following are the findings noted five days after the beginning of the experiment (ten treatments), fourteen days after the beginning of the experiment (twenty-eight treatments) and five days after the last treatment, as indicated in the table:

Three Per Cent Sulfathiazole in Propylene Glycol (p_H 5.1).—During the whole period of treatment this solution produced only slight inflammatory reaction with no or only slight alteration of the olfactory epithelium, which remained insignificant up to the end of the observation period. Some purulent exudate observed during treatment disappeared completely afterward.

Propylene Glycol Alone (p_H 5.4).—This menstruum alone produced no or slight inflammatory reaction in the course of the experiment. No change or only a few small foci of disorganization were seen in the olfactory epithelium, and they promptly disappeared after cessation of treatment. No purulent exudate was seen at any time.

Two Per Cent Diasone in Propylene Glycol (p_H 4.8).—This solution caused considerable inflammation of the mucous membrane, associated with moderate to considerable alteration of the olfactory layer, with excess of mucus and with large amounts of purulent exudate in the nasal cavities, particularly in the frontal openings. These changes became more pronounced as treatment was prolonged. At the end of the experiment the olfactory lining in 2 mice was totally destroyed over rather large areas, with some hemorrhage and ciliary destruction in the mucous membrane of the respiratory portion. However, on the fifth day after cessation of treatment there was some evidence of regeneration; the inflammation was diminished, and the purulent exudate had disappeared. The destructive effect on both the olfactory and the respiratory portion, however, was still marked in some areas at the end of the observation period.

Three Per Cent Diasone in Propylene Glycol with 10 Per Cent Sodium Bicarbonate Added (p_H 8.8).—A slight inflammation was noted within the first five days, and in a few areas there was focal disorganization of the olfactory epithelium, accompanied by large amounts of purulent exudate at both sides of the septum and in the frontal openings. After continual daily treatment, these symptoms became much more marked, while the purulent exudate seemed to disappear. On the fifth day after the last treatment regeneration was evident, and no further changes were seen at this time except some focal disorganization of the olfactory epithelium.

Three Per Cent Diasone in Aqueous Solution with 10 Per Cent Sodium Bicarbonate Added (p_H 8.3).—This preparation caused only slight inflammation, including the respiratory portion of the mucosa, associated with a few foci of disorganization and an excess of mucus in the olfactory portion. In 1 mouse there was an unusually large amount of purulent exudate. This was evident after ten treatments and had not increased when observed after twenty-eight treatments. Return to normal became evident on the fifth day after the last administration.

Two Per Cent Succinylsulfapyrazine in Propylene Glycol with 0.45 Per Cent Sodium Bicarbonate Added (p_H 5.8).—A slight inflammatory reaction was observed with a few foci of disorganization of the olfactory epithelium. This reaction did not become more severe in the following period of administration of the drug. On the fifth day after the last treatment the return to normal was practically complete.

Three Per Cent Sodium Succinylsulfapyrazine in Propylene Glycol (p_H 8.1).—This strength caused about the same slight reaction as the 2 per cent concentration, with only sporadic alteration of the olfactory layer and small amounts of purulent exudate being observed at the end of treatment. Return to normal became evident at the end of the observation period.

Commercial Product Containing Desoxyephedrine and Sodium Sulfathiazole (p_H 9.2).—After ten treatments there were moderate inflammation of the mucous membrane and focal disorganization of the olfactory epithelium, which increased when treatment was continued. After twenty-eight treatments, in some areas this epithelium was thoroughly destroyed; several of these foci of destruction still persisted five days after cessation of treatment, while in other areas regeneration was evident. Large amounts of purulent exudate found in the nasal cavities after ten treatments nearly disappeared in the course of further treatment. An additional mouse that died by accident after six treatme and was replaced in this series, did not s any change at autopsy except slight exces mucus.

Isotonic Solution of Sodium Chloride.—T solution did not cause any change from the n mal. No inflammatory reaction was seen ex for a slight excess of mucus covering the ol tory epithelium.

COMMENT

In varying degree, tissue changes were fo during treatment with all the solutions of fonamide compounds. However, also in vary degree, return to normal was observed in tis specimens taken on the fifth day after the treatment. Our observations indicate that th were marked differences of degree in the inj produced by the various solutions. The le irritation was noted in the series given 3 cent sulfathiazole in propylene glycol (p_H 5. This is in agreement with the experience Yonkman and his associates [3] and with results in human therapy of Blackford.[4] Hum cutt,[5b] using various concentrations of aque solutions of sodium sulfathiazole, obser marked inflammation and purulent exudate o during the first few days; after three days effect in the mucosa was "almost nil."

As mentioned, our 3 per cent solution of s athiazole in propylene glycol, showing slig acid properties, caused only slight and tra tory irritation of the nasal tissue. On the ot hand, the acid 2 per cent solution of diasone propylene glycol, with p_H 4.8, produced highest degree of injury observed in our exp ments. The same compound, diasone, w given in 3 per cent concentration in alkal solution, whether prepared with propylene gly (p_H 8.8) or with distilled water (p_H 8.3), cau a much lower degree of injury than the acid 2 cent solution. While the corrosive effect of th per cent solution appeared still unchanged the fifth day after the last administration, inflammatory reaction caused by the 3 per c solutions was followed by rapid return to norm

Two per cent solution of succinylsulfapyraz (p_H 5.8) and 3 per cent solution of its sodi salt in propylene glycol (p_H 8.1) proved to less irritating than each diasone solution us This was evident notwithstanding the fact th the p_H values of the two solutions were differe the one within the isotonic, or physiologic, ra and the other more alkaline.

Kully [1d] stressed recently that when vasoc strictor drugs are added, particularly to sul thiazole, the irritant properties of the solutio

generally increased. The commercial product aining desoxyephedrine and sodium sulfathie in aqueous solution (p_H 9.2) which we ded in our experiments produced an irrig and partly caustic effect. This effect eased during prolonged administration and followed by slow return to normal.

s reported, bronchopneumonia occurred in 3 of 67 mice, namely, in 2 of the sulfazole group and in 1 of the group given 3 per succinylsulfapyrazine. In these instances y technic may have been responsible rather the drugs contained in the solutions. However, only 1 mouse, belonging to the 2 per cent diasone group, a serious inflammation of the mucous membrane extending beyond the respiratory portion of the nose down to the trachea and the bronchial tract.

SUMMARY

The local toxicity of some solutions of sulfonamide compounds administered intranasally to normal mice was determined by comparing microscopically the affected nasal tissues with normal nasal tissues during and after prolonged administration. The findings were correlated

ologic Changes of the Nasal Mucous Membranes of Normal Mice After Prolonged Local Administration of Solutions of Sulfonamide Compounds

Compound Used	Concentration, %	Solvent	p_H	Pathologic Changes *		
				After 5 Days of Treatment	After 14 Days of Treatment	5 Days after the End of Treatment
.....	..	Isotonic solution of sodium chloride	7.2	Inf. —	—	—
				Olf. —	—	—
				Pus —	—	—
.....	..	Propylene glycol	5.4	Inf. —	(+)	(+)
				Olf. +	+	(+)
				Pus —	—	—
Sulfathiazole.....	3	Propylene glycol	5.1	Inf. (+)	(+)	(+)
				Olf. (+)	(+)	(+)
				Pus +	+	(+)
Diasone.....	2	Propylene glycol	4.8	Inf. ++	+++	+
				Olf. ++	+++	+++
				Pus ++	++	—
Diasone.....	3	Propylene glycol with 10% sodium bicarbonate added	8.8	Inf. +	++	—
				Olf. +	++	+
				Pus ++	(+)	—
Diasone.....	3	Distilled water with 10% sodium bicarbonate added	8.3	Inf. +	+	(+)
				Olf. +	+	(+)
				Pus ++	+	—
Succinylsulfapyrazine.....	2	Propylene glycol with 0.45% sodium bicarbonate added	5.8	Inf. +	+	(+)
				Olf. (+)	+	+
				Pus +	+	—
Sodium succinylsulfapyrazine	3	Propylene glycol	8.1	Inf. +	+	(+)
				Olf. +	+	+
				Pus —	+	(+)
Commercial product containing sodium sulfathiazole and desoxyephedrine		Distilled water	9.2	Inf. +	+	+
				Olf. +	++	++
				Pus ++	(+)	(+)

Inf. signifies an inflammatory reaction of the mucous membrane; Olf., pathologic changes of the olfactory epithelium; purulent exudate found in the nasal cavities. A negative sign indicates that there was no change; (+), a few sporadic elial changes; +, slight damage of tissue; ++, moderate, and +++, excessive damage.

r, Hunnicutt,[5c] judging from his experiment mice, had the impression that whenever there a considerable amount of purulent exudate he nasal cavities of the mice, purulent bronis or bronchopneumonia was produced. He cluded that a continual severe disturbance the nose will usually cause inflammatory nges also in the lower respiratory tract. This estigator administered various concentrations sodium sulfathiazole three times daily for days as we did twice daily for fourteen days. we reported, during treatment we observed, ier frequently, large amounts of purulent date in the nasal cavities, sometimes in the uses also. However, aside from the aforemened bronchopneumonia in 3 mice, at the end the period of treatment there was found in

with the various p_H values of the preparations used.

Three per cent sulfathiazole in propylene glycol with a p_H value near the normal physiologic range of nasal secretions in man showed the least irritating effect. Propylene glycol alone did not show any detrimental effect nor did isotonic solution of sodium chloride.

The greatest injury and a slow return to normal were observed with a 2 per cent diasone solution in propylene glycol, which showed the highest acidity among the solutions used (p_H 4.8). However, return to normal was observed on the fifth day after the last administration.

The succinylsulfapyrazine solutions used caused smaller inflammatory reactions than did

the 3 per cent diasone solutions, and cessation of the treatment was followed by more rapid return to normal. There were no differences observed with the two succinylsulfapyrazine solutions, one of which was slightly acid and the other slightly alkaline.

One of the commercial preparations, which is a combination of desoxyephedrine and sodium sulfathiazole in aqueous solution of p_H 9.2, was included in the experiment. It caused inflammatory and partly caustic effect du treatment, followed by slow return to nor

In our experiments it was observed that 2 per cent diasone solution, which had acid p erties, with p_H below 5, caused much gre damage than the 3 per cent solution of the s compound, which was alkaline, with p_H 8.8.

2101 Pine Street.

HISTOLOGIC OBSERVATIONS ON THE HEALING OF LABYRINTHINE FISTULAS IN MONKEYS

J. R. LINDSAY, M.D.
CHICAGO

urgical procedures for the relief of deafness to ankylosis of the stapes have been conred and carried out almost since the pathoc process became recognized.

n the latter part of the last century several hods were tried without success, such as reval of a part of the drum, removal of the outer cles and manipulation of the stapes in the e of overcoming the interference with sound duction. The possibility of restoring hearing reating a fistula in the bony wall of the labyh was also considered, and in 1876 Kessel [1] mpted extraction of the stapes, hoping to ain in its place a thin movable membrane covg the oval window.

Extirpation of the stapes proved to be imcticable because of the technical difficulty in mplishing the objective, since the crura ally fractured. It was also discouraging bese of failure to obtain a lasting improvement earing and the danger of infection. Twenty rs later Passow [2] attempted the creation of a ula by drilling through the promontory near oval window with a trephine. He obtained improvement in hearing which, however, ed only a few days.

The further development of operations for creation of an opening into the labyrinth by ány, Jenkins, Holmgren and Sourdille has n accurately outlined by Holmgren [3] and Engstrom.[4] Holmgren's work included a procedure in which the microscope was introduced during operation. He also made a careful investigation of several locations and types of covering for the fistula. While improvement was obtained in the duration of the hearing gain, ultimate closure was apparently the rule, although the fistula sometimes was present for periods of several months. On the basis of Holmgren's work, Sourdille [5] then developed the use of a thin epithelial flap of epidermal origin to cover the fistula and met with success in keeping the fistula open for periods of years.

The possibility of maintaining an apparently permanent fistula in the bony wall of the horizontal semicircular canal has since been repeatedly demonstrated by Sourdille [5] and by Lempert [6] and his followers. The method has consisted basically in using a flap of thin skin free from glands to cover a carefully prepared fistula that exposes the membranous canal.

While success has been reported in varying percentages, the incidence of failure continues to be high and the degree of hearing improvement to be widely variable.

The chief cause of the gradual loss of the hearing improvement continues to be the closing of the fistula by new bone.

From the Division of Otolaryngology, University of cago.

This work was aided by a grant from the American logical Society.

Presented before the Otosclerosis Study Group at annual meeting of the American Academy of thalmology and Otolaryngology, Oct. 8, 1944.

1. Kessel, J.: Ueber die Durchschneidung des gbügelmuskels beim Menschen und über die Extrac- des Steigbügels, Arch. f. Ohrenh. **11**:199, 1876.

2. Passow, K. A., in discussion on Panse: Die rative Behandlung hochgradiger Schwerhörigkeit, handl. d. deutsch. otol. Gesellsch. **6**:14, 1897.

3. Holmgren, G.: Surgical Therapy in Otosclerosis, Nelson's Looseleaf Surgery of the Ear, New York, s. Nelson & Sons, 1938, chap. 17.

4. Engstrom, H.: Ueber das Vorkommen der Otosklerose nebst experimentellen Studien über chirurgische Behandlung der Krankheit, Acta oto-laryng. 1940, supp. 43, p. 1.

5. Sourdille, H.: New Technique in the Surgical Treatment of Severe and Progressive Deafness from Otosclerosis, Bull. New York Acad. Med. **13**:673 (Dec.) 1937.

6. Lempert, J.: Improvement of Hearing in Cases of Otosclerosis, Arch. Otolaryng. **28**:42-97 (July) 1938; Endaural Fenestration of External Semicircular Canal for Restoration of Hearing in Cases of Otosclerosis, ibid. **31**:711-779 (May) 1940; Endaural Fenestration of Horizontal Semicircular Canal for Otosclerosis, Laryngoscope **51**:330-362 (April) 1941; Fenestra Nov-Ovalis: New Oval Window for Improvement of Hearing in Cases of Otosclerosis, Arch. Otolaryng. **34**:880-912 (Nov.) 1941; Lempert Fenestra Nov-Ovalis with Mobile Stopple, ibid. **41**:1-41 (Jan.) 1945.

Animal experimentation has contributed information regarding the process of healing of fistulas but has been less productive of practical help in the prevention of bone regeneration.

The monkey has usually been selected for experimentation because of the similarity of the anatomic arrangement to that of man, but the smallness of the parts has undoubtedly been a great factor in the inability to reduplicate the results obtained in human subjects.

Experiments made on monkeys by Holmgren,[3] Engstrom[4] and Fowler Jr.[7] have shown a constant tendency of the fistula to be fairly rapidly closed by new bone. More recently Shambaugh Jr.[8] has been able to prevent bony closure in the monkey for longer periods by a technic similar to that used in the human subject. Holmgren[3] and Engstrom[4] tried a variety of methods and materials for covering the fistula. These included such tissues as dura mater, mucoperiosteum, lenticular capsule, muscle, fat, foreign substances such as gold foil, rubber, Laminaria rod and Kerr's Compound,[8a] grafts of epidermis and the thin skin of the bony part of the external auditory canal. New bone grew in from the periosteal surface to cover the fis in all cases. Retardation of such bony ingro was noted when the fistula was exposed radium and when stratified epithelium was u but mesodermal tissue seemed to be a good stratum for the newly formed osseous tissue.

Canfield[9] noted a delay in new bone forma following the use of the polishing burr as c pared with the chisel and considered that p vention of bony regeneration depended on method of dealing with the bone rather than the type of covering used. While Nager,[10] Ho gren[3] and Engstrom[4] interpreted bony clos as originating mainly from the periosteal s face, Fowler Jr.[7] directed attention also to osteogenetic activity of the endosteal layer.

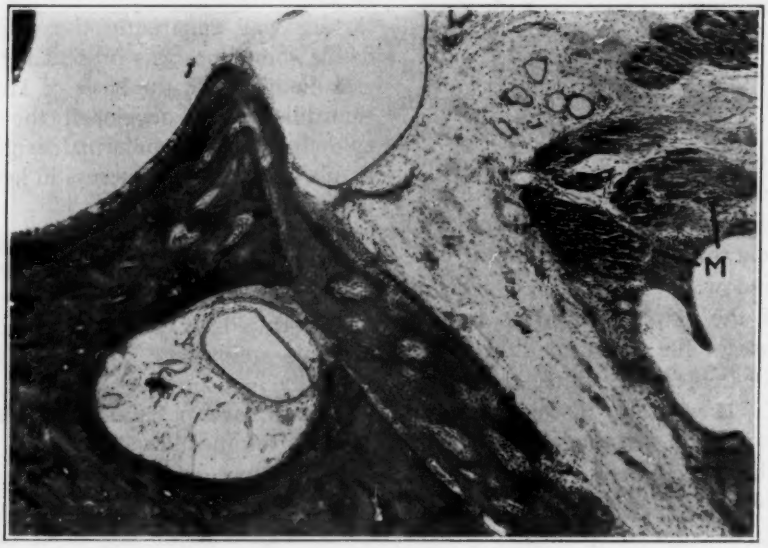


Fig. 1.—Fistula of forty-two days' duration in the right ear of monkey 16. The conjunctival graft pla over this fistula has degenerated, and the muscle (*M*) used to hold it in place has not inhibited regenera of bone. The callus is mainly periosteal in origin, with a seam of endosteal bone at one margin, where endosteum was stripped at operation. The saucer-shaped depression is unfavorable for successful applica of a covering flap.

EXPERIMENTAL MATERIAL, TECHNIC AND OBJECTIVES

The present report comprises preliminary obser tions on a small series of monkeys' ears operated in 1940 and 1941 and a second series of 48 ears opera on over a two year period up to the beginning of 19

As to the latter series, the histopathologic obser tions are completed in approximately half the ea in the others only the clinical results as indicated the test for presence of a fistula are as yet availab

The objective in these experiments has been to st the process of bone regeneration at the site of

7. Fowler, E. P., Jr.: Critique of Surgical Treatments for Deafness, Canad. M. A. J. **43**:546-552 (Dec.) 1940.

8. Shambaugh, G., Jr.: Scientific Exhibit, American Academy of Ophthalmology and Otology, Chicago, October 1944.

8a. Kerr's Compound is a waxlike material used in dentistry for taking impressions of the mouth. It is a proprietary preparation.

9. Canfield, N.: Labyrinthine Fistulas: Report Experiments on Vital Response to Various Meth of Producing Defects in Bone, Arch. Otolaryng. 50-62 (July) 1939.

10. Nager, F. R.: Demonstration zur Holmgrensch Otoskleroseoperation an Affen, Acta oto-laryng. 350-358 (July-Aug.) 1939.

and factors which might exert an inhibitory on such regeneration.

cause of the technical difficulty of carrying out in exact procedures on the monkey, the more e experiments were attempted first, and those pro-es which were technically more difficult were yed until later. Each fistula was made with a ing burr, usually in a moist field under a dissec-microscope. Removal of bone dust and endosteum done with fine needles and intermittent irrigation. fistula was made in the horizontal semicircular in all cases, the location varying with reference e ampulla. In a few the posterior canal was also ed.

e type of covering used was confined to some of cutaneous flap or graft and to conjunctival s.

g. 2.—Fistula of two weeks' duration in the left of monkey 11. Callus is developing from both the steal and the endosteal surface. The cutaneous reflected from the posterior wall of the external tory meatus failed to prevent regeneration of steal bone. Small bone fragments have also de-sed the membranous canal. Eventual closing of the la by endosteal bone is thereby assured indepen-ly and has already begun at the margins of the la beneath the stripped endosteum.

e observations to be presented include the follow-(1) the normal process of healing, (2) factors h influence osteogenesis from the periosteal layer (3) factors which influence osteogenesis from the steal surface of the capsule.

THE NORMAL PROCESS OF HEALING

n all the early experiments, proliferation of a r of osteogenic connective tissue occurred between the covering flap or substance and the bony surfaces, extending into the lumen of the semicircular canal to varying degrees beyond the margins of the fistula (fig. 1). New bone appeared about the sixth day and was laid down along the cut bony surfaces of the capsule or on bone fragments which happened to lie in the proliferating tissue.

A thick callus usually had formed within two weeks (fig. 2). When the fistula had been made on the prominent part of the canal near the ampulla, the callus was usually thinner than when the fistula lay at the bottom of a concavity facing the antrum of the mastoid process.

The chief source of the proliferating osteogenic tissue appeared to be the deeper or cambium layer of the periosteum and possibly haversian canals. The enchondral layer routinely showed little sign of proliferative activity, probably because of the scarcity of vascular channels, but as new bone was laid down, it appeared first along the cut surface of the bony capsule or against bone fragments, later as irregular processes throughout the osteogenic tissue.

New bone also appeared at the margin of the fistula between the endosteum, which was invariably stripped off slightly, and the endosteal surface of the bone. The degree to which proliferation of osteogenic connective tissue occurred within the lumen of the canal varied greatly, depending on factors to be discussed later.

In general, proliferation of new bone of periosteal origin appeared to be more rapid and chiefly responsible for early bony closure of the fistula, while closure of endosteal origin proceeded more slowly.

Definite differentiation between new bone growing in from the periosteal surface and endosteal bone could be made only where ingrowth of periosteal bone had been partially or wholly excluded. In the early experiments the latter was never accomplished, and closure always appeared to occur primarily from the periosteum.

Resorption of the callus appeared to be slow, extending over a period of months. Osteoclasts were usually scarce but in a few cases were more abundant. As resorption proceeded over a period of months, it also involved the margins of the enchondral layer, which had formerly appeared as a smooth surface, and occasional pockets appeared as well as enlarged vascular channels extending into this layer. Eventually these pockets and channels became filled with new lamellar bone, so that the former cleancut margins were interrupted and a firmer union with the enchondral capsule was created (fig. 4 *B* and *C*).

More extensive resorption of the endosteal and enchondral layers occurred along vascular channels whenever the perilymphatic space was filled by new bone. In many of these the periosteal bone had been excluded successfully by the covering of the fistula, so that the impression was given that the stimulus which led to extensive regeneration of endosteal bone also involved the surrounding endosteal and enchondral bone the capsule (figs. 5 *A*, 6 *A* and *B* and 7 *B*).

The extent to which regeneration of b occurred from the endosteum could be de mined with some assurance only in those ear which periosteal bone had been successf impeded or excluded.

Bone regeneration of endosteal origin apparently dependent on several factors, the m

Fig. 3.—*A*, fistula in the right ear of monkey 3 at twenty-nine days. Periosteal bone has been prevented in growing across the fistula by the Thiersch graft. The lumen is filled by connective tissue and small bo chips, and new bone is appearing in apposition to the bony walls. Trauma of the endosteal lining and m ture of the membranous canal, which occurred in the effort to pick out bone fragments with the needle, of a probable explanation for this proliferation of osteogenic tissue. The bone fragments contain no liv cells and play a passive role. The regeneration of bone following endosteal injury occurs more slowly th that which originates from the periosteum.

B, fistula in the left ear of monkey 8 at thirteen months. The fistula remains open although the epider covering has been lost in the histologic preparation. A hair fragment was incorporated in the new bone at t margin (arrow). The perilymphatic space is filled by new bone. At a more distal point the membranous ca was collapsed, but beyond the region of the fistula the labyrinth appeared histologically normal. The fistul reaction was positive for ten and a half months but was not obtained thereafter for some unexplained reas A Thiersch graft was used.

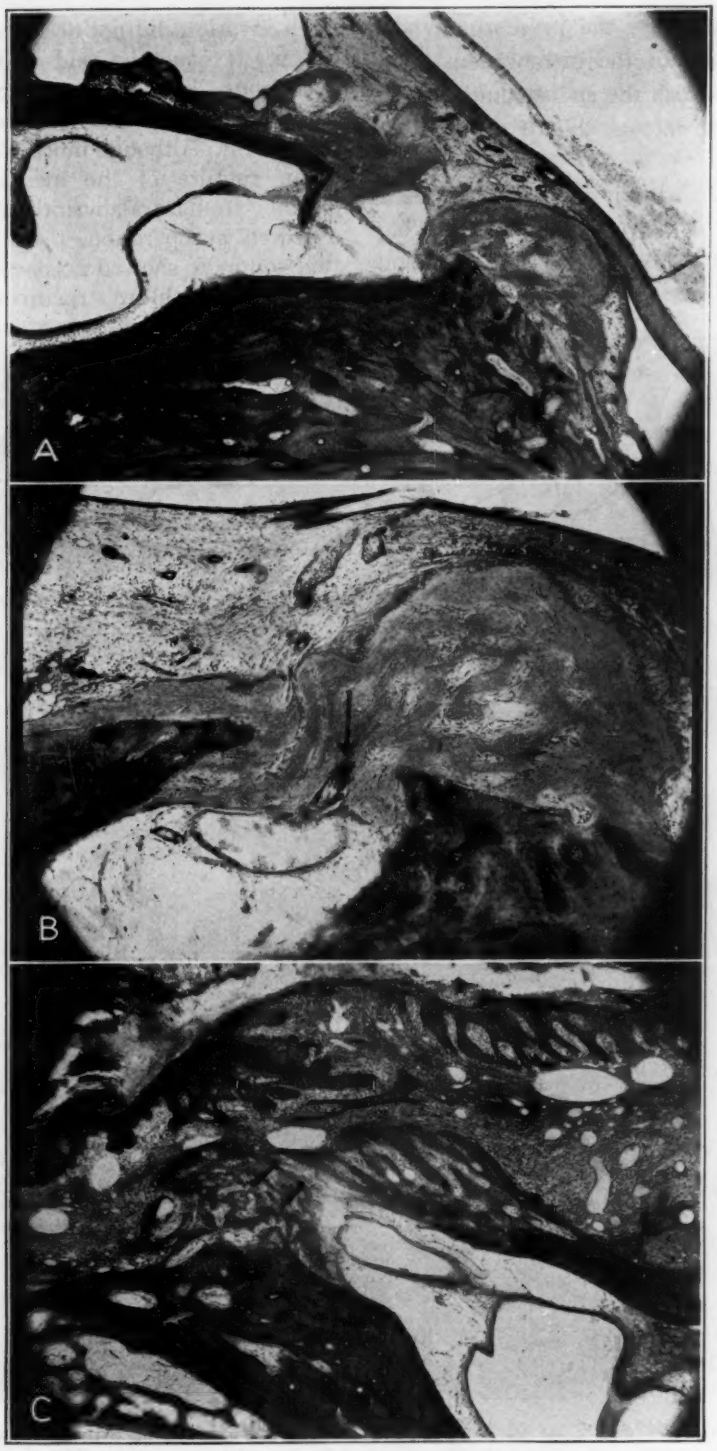


Fig. 4.—*A*, fistula in the right ear of monkey 20 at one hundred and twenty-nine days. The fistula test strongly positive. Although the fistula has not closed, a localized mound of callus has formed at the gins elevating the covering flap of skin. The skin contains glands and hair follicles. A depressed frag- of bone was left attached by endosteum and is now incorporated in new bone. Such fragments distort membranous canal. Their removal without trauma is difficult.

B, section through the same fistula. In this area the localized mound of callus covers the fistula, in the er of which a fragment of hair is incorporated (arrow).

C, fistula in the right ear of monkey 15 at one hundred and five days. The fistula test evoked a strongly tive response at sixty-six days; it was not made thereafter. The animal died from meningitis, apparently genous but not due to bacterial invasion of the labyrinth. Localized mounds of callus have formed at the es of the fistula, in which fragments of hair (arrows) are seen. Closure has become almost complete. Such ments result from cutting through hair follicles in the preparation of the graft and appear to stimulate the duction of callus.

important of which were the presence of bone fragments, the state of the membranous canal and the extent to which the endosteum had been traumatized. These factors will be discussed in some detail later.

Diffuse bacterial invasion of the labyrinth was rare but did occur in at least three ears as a late complication several months after operation. Studies of these ears are not yet completed. Such invasion did not occur as an early com cation. It could be said that with these t exceptions histologic evidence of intral rinthine damage beyond the region of the fis was absent. Although much trauma of the en teum, rupture of the membranous canal bleeding from intralabyrinthine vessels were o observed at operation, the histologic exam tion routinely showed no obvious evidence o jury to the cochlear structures.

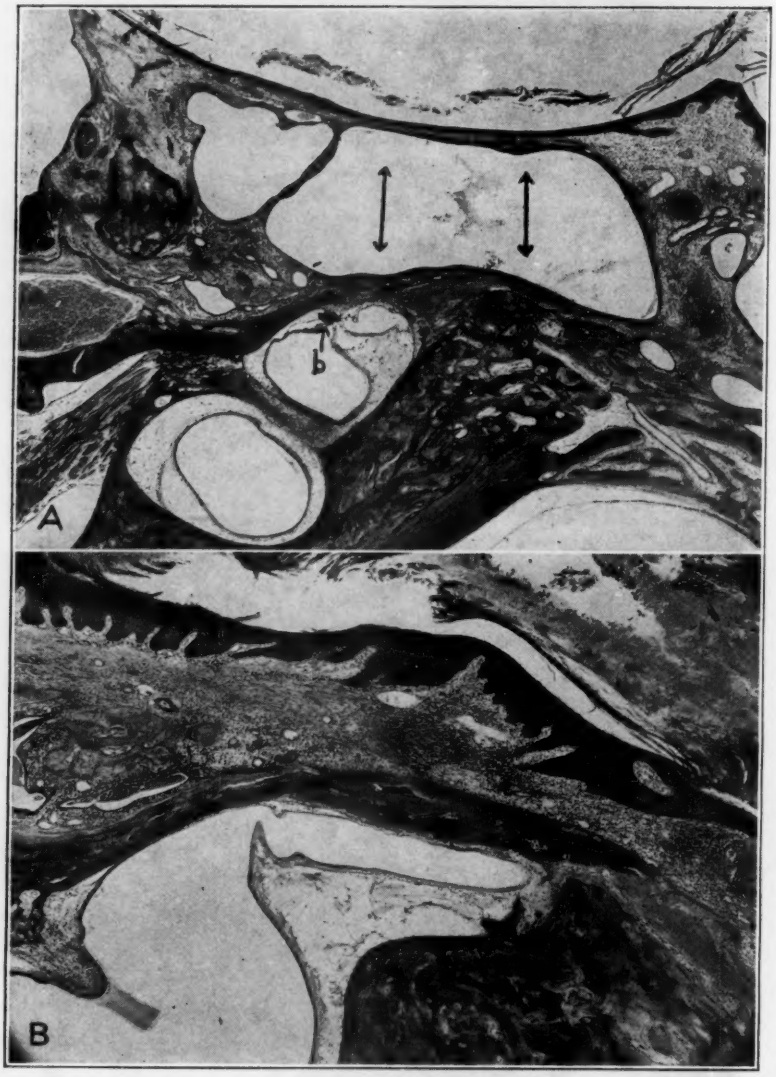


Fig. 5.—*A*, fistula in the right ear of monkey 25 at ninety-five days. The fistulous reaction was moderat active at the time the animal was put to death. The fistula has almost closed. The dermal graft has li but the skin has been lifted away from the fenestra (arrows) by an air pocket extending from the middle Inadequate removal of the posterior rim of the annulus tympanicus and of the posterior wall of the exte auditory meatus predisposes to such an occurrence, since the fistula then lies at the base of a narrow re Additional factors promoting bony closure here are the depression and distortion of the membranous c caused by a bone fragment (*b*) and rupture of the canal at a more distal point with bony obliteration o lumen.

B, fistula in the left ear of monkey 25 at seventy-three days. The fistulous reaction was positive. Altho this reaction was positive, a thin layer of callus covers the fistula completely. It appears that open vasc spaces which are present in the callus at an early stage may permit transmission of pressure to the membran labyrinth. The failure to prevent bony closure appears to have been due to partial degeneration of the g and infection. The epidermis extended barely across the fistula.

TORS WHICH INFLUENCED OSTEOGENESIS FROM THE PERIOSTEAL LAYER FOLLOWING VARIOUS PROCEDURES

The cutaneous flap to cover the fistula was cted from the posterior wall of the external tus, the ossicles, the tympanic membrane the bony bridge having been left in place; packing was used for five to eight or more (7 ears).

The fistulas in these 7 ears closed rapidly. e were known to remain open for more than ut two weeks.

While the factors tending to promote regeneration of bone were several, and not limited to the manner of covering the fistula, it was striking that a layer of callus of periosteal origin developed rapidly in every instance.

The epidermal layer of the flap was always found to be widely separated from the fistula. The layer of callus appeared however to be thinner than when no epidermal flap was used, indicating some inhibitory influence. (See figure 2.) A cause of failure may have been a tendency for the flap to pull away from the fistula after

Fig. 6.—*A*, fistula in the right ear of monkey 4 at thirteen months. The fistulous reaction was positive ten months. The conjunctival graft is no longer recognizable. The fistula has not closed although it is owed by two distinct layers of new bone (arrows). Spontaneous nystagmus occurred at six months, sug- ing labyrinthitis, but a reduced fistulous response persisted for four months thereafter. The mem- ous canal and sense organs have been destroyed by labyrinthitis. See *B*.
B, section through the vestibule and the cochlea of the same ear. The soft tissue structures have been royed, and ossification is advancing. A fistulous tract is seen leading into the vestibule through the oval dow. The stapes is dislocated. The cause of the labyrinthitis has not been determined, but traumatic cation of the stapes is suggested by the histologic appearance.

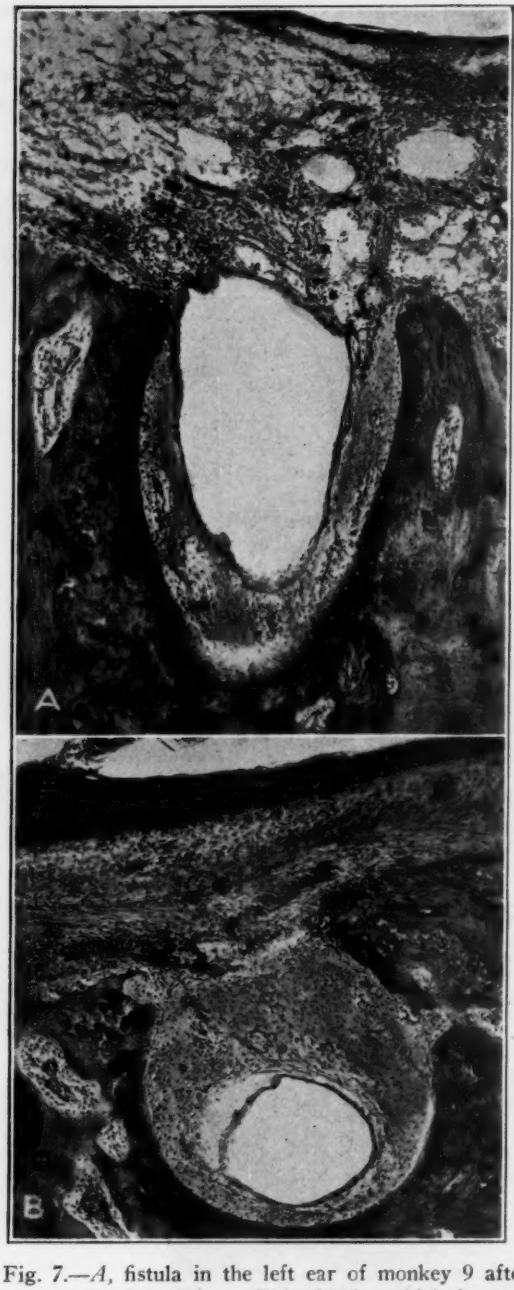


Fig. 7.—*A*, fistula in the left ear of monkey 9 after forty-two days' duration. This fistula, which is open at six weeks, was covered by a conjunctival flap with epithelium toward the fistula, held in place by a cutaneous flap reflected from the posterior wall of the external auditory meatus. The conjunctival epithelium shows degeneration. Periosteal bone has been effectively excluded, but the perilymphatic space is obliterated by new bone of endosteal origin. See *B*.

B, another section from the same fistula. In this region, the membranous canal is depressed, and the new bone forms a complete ring around it. At a slightly distant point the membranous canal has been obliterated.

Erosion of the endosteal and enchondral layers of the capsule along vascular channels is shown here. Absorption of the enchondral layer of the capsule is a characteristic finding when the perilymphatic space has been obliterated by new bone.

removal of the packing or during fibrous ti contraction, since the fistula lay at the botto a concavity. The cutaneous flap itself, the u surface of which consisted of reflected pe teum, did not show regeneration of bone. W for instance, a conjunctival or a cutaneous g was placed between the flap and the fistula, bone appeared only in apposition to old b never between the graft and the covering fla

In this group of ears rapid closure had curred from periosteal bone. In the ligh later experiments, however; other factors w present which would have caused eventual clo by bone of endosteal origin (fig. 2), but c closure would usually have been slower in de opment.

2. A thin Thiersch graft was taken from scalp to cover the fistula (18 ears).

Such a graft could have been expected prove undesirable because of hair follicles glands, many of which were cut through, that fragments of hair occasionally got bene the graft. For purposes of study, however, Thiersch graft was useful.

The graft was held in place in most insta by a cutaneous flap reflected from the poste wall of the external meatus, and in a few muscle, with firm packing for periods of a w or more.

In one third of the ears the graft degenera and in these ears bony closure of the fistula the rule.

Several fistulas remained open until the m keys were killed at four and five months; was patent for ten months (fig. 3 *B*). In some these animals the periosteal bone seemed to h been effectively impeded or prevented fr growing over the fistula (fig. 3 *A*), but di factors were present which promoted regene tion of endosteal bone.

In several ears in which gradual closure curred within three to five months, small fr ments of hair were found beneath the flap, s rounded by an excessive amount of cal Apparently the formation of callus was stimula by the fragments of hair, so that a localiz mound resulted at the fistula. Although bo closure had not become complete in some these ears, eventual closure might be expec (fig. 4).

A progressive reduction in the activity of response to the fistula test was observed in so of these ears over a period of several weeks fore closure was complete. In several instan in which the response was greatly decreased fore the animal was killed, the new bone found to extend all the way across the fist

(c) Other procedures:

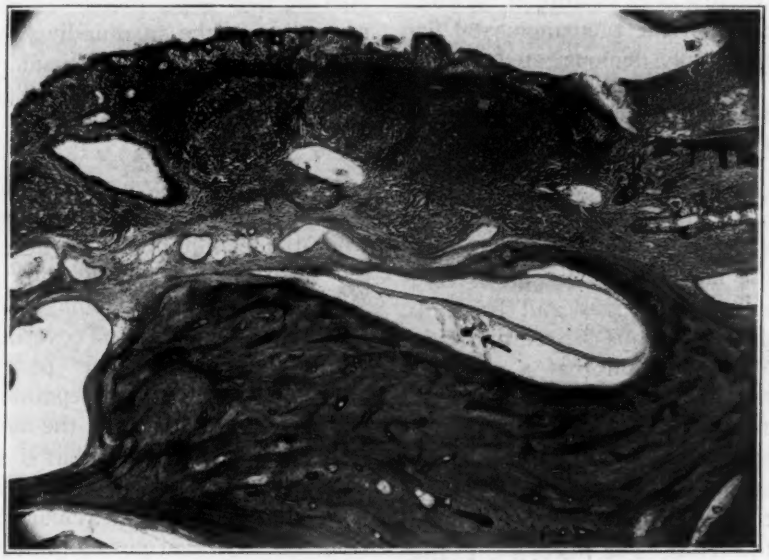
When the membranous canal was inta

5 *B*). The persistence of a weak fistulous onse after the callus had covered the fistula apparently explained by the wide vascular es which in the early stages of callus forma- permitted some transmission of pressure.

econdary infection of the cavity of the toid process was the general rule in the keys of this group. It is possible that in e ears an inflammatory reaction in the sub- helial layer of the covering may have con- ted to closure (fig. 5 *B*).

hese experiments demonstrated the unde- ble tendency of Thiersch grafts to degenerate particularly the adverse effect of fragments air in promoting callus formation. On the hand, they showed the possibility of pre- open at the time the animal was killed at thirteen months (fig. 6).

In a third ear closure occurred by ingrowth of periosteal bone. In the remaining 2 ears, histologically examined at six weeks, the graft had lived and periosteal bone had been prevented from growing over the fistula (fig. 7). The chief point of interest in this group is that the possibility of inhibiting or preventing the ingrowth of periosteal bone has been demonstrated. When these conjunctival grafts were compared with Thiersch grafts used in a similar manner, the results appeared to be improved. In this group of ears factors which influenced the regeneration of bone of endosteal origin were demonstrated, which will be discussed under that heading.



ig. 8.—Fistula in the right ear of monkey 30 after a duration of one hundred and sixty-three days. The or fistula evoked a 4 plus reaction. The conjunctival graft placed with epithelium outward has been pre- d. The point of junction with skin is shown at the right. There is no sign of active regeneration of bone at margins of the fistula. The covering flap is attached to the membranous canal and separated from the peri- hatic space by it and new bone along the margins of the fistula. A small bone fragment has slipped down the perilymphatic space and is fixed there by loose connective tissue (arrow).

ing ingrowth of periosteal bone for periods least several months.

Conjunctival grafts were used, held in place reflected flap of skin plus packing for ods varying from six days to as long as months.

) Conjunctival graft with epithelium toward one (5 ears). The graft was held in posi- either by a cutaneous flap or by muscle re- ed from the posterior wall of the external tus. The packing was left in place for periods ing from six days to two months.

2 of these 5 ears the graft had apparently nerated to the point that the epithelium d not be recognized; in one the fistula had d, while in the other it was histologically

(*b*) Conjunctival graft with epithelium outward; graft held in place by a reflected flap of skin and packing. One ear was treated in this manner. The packing was left in place for more than two weeks and at the time of histologic examination, after five months, the fistulous response was active and the fistula completely open (fig. 8).

This graft showed no evidence of degeneration, whereas when the epithelium was turned to the bone, progressive degeneration of the epithelium occurred.

The encouraging results obtained with conjunctival grafts have warranted further investigation of this type of covering for the fistula.

Their presence promotes bony obliteration of the perilymphatic space always

(*c*) Other procedures:

A graft of skin from the bony external meatus was used to cover the fistula.

A tympanomeatal flap of skin was employed according to the Lempert technic.

Roentgen radiation was used after operation.

Since presentation of this preliminary report the cartilaginous stoppel has been used in a further series.

Since the histologic observations are only partly available, these groups are not included in this preliminary report. It may be stated, however, that in animals in which the tympanomeatal flap was used the response to the fistula test has remained active in some ears until autopsy of the animals at fourteen months. The possibility of preventing bony closure in the monkey's ear by the use of the tympanomeatal flap has therefore been amply demonstrated.

FACTORS WHICH PROMOTE AND THOSE WHICH INHIBIT OSTEOGENESIS FROM THE ENDOSTEAL SURFACE

1. *Endosteum.*

Osteogenic tissue proliferating from the endosteal surface of the labyrinthine capsule is commonly observed in labyrinthitis and fractures. Certain cases of mild serous labyrinthitis, for instance, give the impression that a relatively mild irritation may promote osteogenic activity of the endosteum.

In order to determine the effect of leaving the endosteum across the fistula, an effort was made in several ears to remove all bone dust without removing the endosteum. The histologic examination of these ears always showed thin flakes of bone remaining along with the endosteum and thereby providing an ideal framework for proliferation of endosteal bone. When all bone dust and flakes were removed, the endosteum was torn away also. In the monkey it did not appear possible to remove all bone without also removing the endosteum. Some degree of stripping of endosteum from the bone beneath the margins of the fistula was the rule, and thereby was created the possibility of marginal proliferation of osteogenic tissue. In many ears new bone completely obliterated the perilymphatic space in the region of the fistula; beyond this area that space was normal (figs. 3 and 7). The most probable explanation for this ossification appeared to be the trauma done to the endosteal lining in the removal of bone fragments. This could occur both from the point of the needle and from the sharp fragments themselves, which would often slip inside the bony margins during the attempt to tear them free.

When the membranous canal was intact lumen was apparently not encroached Whether or not the new bone of endosteal extended between the membranous canal an covering of the fistula appeared to depe whether or not the membranous canal was to assume its normal position in apposition t outer periphery and hence in contact wit covering placed over the fistula. (Compa and *B* in figure 7.)

Under such conditions obliteration of perilymphatic space by new bone in the r of the fistula was shown to be compatible maintenance of an open fistula (figs. 3*B* 7*A*).

When the perilymphatic space was ob ated by new bone, there was usually also resorption of the surrounding endosteal an chondral layers of the capsule, along vas spaces. Eventually new lamellar bone wa posited along these spaces (figs. 5*A*, 6*A* a and 7*B*).

It has been a consistent finding in these that an open fistula has been maintained when the membranous labyrinth became fix the covering flap without intervention of l When no part of the membranous labyrinth found in contact with the covering flap, new always developed. The perilymphatic s always has been found separated from the either by new bone or by the membranous c

It appears, therefore, that if a fistula is t kept open, it must be placed along the periphery of the semicircular canal, where membranous canal normally hugs the bony and therefore makes contact with the flap. loose connective tissue attachment between membranous canal and the endosteum is ser in the preparation of the fistula, and this pe healing and fixation of the covering flap to membranous canal.

Any effort to create a permanent opening the vestibule, for instance, or along the l curvature of a semicircular canal, if it technically feasible, could therefore not expected to succeed, because the membra labyrinth would not make contact with the co ing flap, and regeneration of endosteal would be uninhibited.

2. *Bone fragments.*

The bone fragments and dust consist ma of enchondral and endosteal bone. Larger fr may carry endosteum, and some may stil attached by endosteum at the margins of fistula (figs. 3*A* and 4*A*). Such loose f ments always show loss of the nuclei of the cells and probably have no active part in

neration. Their presence promotes bony re of the fistula through their effect in de- ing the membranous canal and thereby cre- a space in which osteogenic tissue may erate.

e new bone is deposited early along such ents as well as against the polished bone e margins of the fistula. Small fragments lie free in the perilymphatic space at some nce from the traumatized margins of the a may be fixed in position by a few strands ose fibrous tissue without new bone forma- (fig. 8).

mplete removal of all bone fragments is tial to permit complete contact between the ing flap and the membranous canal. How revent small fragments from slipping be- the margins at the ends of the fistula and by depressing the membranous canal proved one of the main problems in preparing the a.

Condition of the membranous canal.

y depression of the membranous canal as ult of the presence of bone fragments favored growth of bone between the canal and the ring flap. If the covering flap failed to ex- periosteal bone, the fistula was closed over ly, but when periosteal bone could be pre- d from growing in, any closure which oc- d by proliferation of bone from the endo- margins between the depressed canal and flap usually required a much longer period. terruption in the continuity of the mem- ous canal was frequently found. This was ys associated with displacement of the torn usually depression but sometimes evulsion. rs showing this damage of the canal the peri- hatic space in the region of the trauma was ys obliterated by new bone. In several of ears, however, the fistula remained open . 3*B*, 4*A* and 7*A*), the membranous canal e end of the fistula having healed to the ring flap.

herever depression or separation of the branous canal from the flap occurred, a of osteogenic tissue and eventually bone loped between (fig. 7*B*).

e reason for the frequent interruption of nuity of the membranous canal found on logic examination is not clear since trauma g surgical procedure was not recognized; ever, the almost complete transparency of structure in the monkey sometimes made it ult even under a microscope to determine her the canal had been ruptured. In cases hich the canal was known to be damaged, obliteration of the perilymphatic space always occurred, and ossification progressed slowly.

Although a positive fistulous reaction and a histologically normal cochlea were observed in animals with an interrupted membranous canal, no information was available as to the state of the auditory function.

The membranous canal of the monkey is more transparent and appears to be more easily damaged than that of the human being.

There may have been other factors, in addition to those listed, contributing to the effect on bone regeneration in these ears. For example length of time and degree of firmness in applying packing are probably of importance. The manner of preparing the cavity is undoubtedly an essential not only to obtain a dry cavity but to allow favorable application of the covering flap and to avoid such a complication as that shown in figure 5*A*. It is possible that the chief advantage to be gained from the use of tissue from an external surface, such as conjunctiva or skin, lies in the protection and stability which it provides after having once been fixed in position by the process of healing.

The greatest problem in these experiments has been to separate clearly the different factors contributing to the end results. Because of difficulty in carrying out the technics so precisely as to permit of a single variable, with all other factors controlled, it has been necessary to do many operations and to select the material which affords the best evidence.

It has not been possible to determine auditory function in these animals, but a correlation between the degree of response to the fistula test and the histologic picture has been demonstrated.

SUMMARY

The results which are now available from the first half of this series of fenestration operations on monkeys seem to warrant the following interpretations regarding the regeneration of bone at the fistula.

1. The fistula in the bony semicircular canal always closes by formation of new bone unless certain measures are carried out.

2. The regeneration of bone occurs rapidly from the periosteal layer and more slowly from the endosteal surface of the capsule. Complete closure may occur from either or both layers.

Attempts to prevent regeneration of periosteal bone have resulted as follows:

1. The use of a cutaneous flap reflected from the posterior wall of the external auditory

meatus without removal of the annulus tympanicus was not successful. The situation of the fistula in a concavity tends to prevent close contact with the covering flap throughout the healing period.

2. Thiersch grafts of hair-bearing skin were frequently successful in preventing closure for several months but proved to be unsatisfactory because of occasional degeneration and because of the presence of hair fragments beneath the graft, which stimulated formation of callus and eventual closure.
3. Conjunctival grafts were used with a sufficient degree of success to warrant further laboratory investigation.
4. The use of a tympanomeatal flap according to the Lempert technic has given the best results as indicated by the response to the test for fistula. A further report on this series as well as on the use of a cartilaginous stopple will be possible when histologic preparations are finished.

A factor predisposing to success in the application of any covering graft or flap is the locating of the fistula on a convex surface rather than in a localized concavity. Such a site is obtainable slightly distal to the ampulla when the pos bony wall of the external auditory meat the rim of the annulus tympanicus are adeq removed.

The evidence suggests that any fistula re open only by virtue of the union which between the membranous labyrinth and the ering flap to the exclusion of osteogenic The perilymphatic space always becomes rated from the covering flap either by a la new bone or by the membranous laby Measures necessary to permit fibrous unio tween the membranous labyrinth and the ing flap have been shown to be:

1. Bone fragments and endosteum m completely removed from the fistula
2. The normal contour and position membranous canal must be preserv that it makes uninterrupted contact the covering flap.

Failure in this was commonly caused by ing bone fragments to slip between the bon the endosteum or between the endosteum the membranous canal and by injuring or turing the membranous canal, so that it b depressed or displaced.

950 East Fifty-Ninth Street.

ONCHOSCOPY AS AN AID IN THE DIAGNOSIS AND TREATMENT OF ALLERGIC PULMONARY DISEASE

WILLIAM A. LELL, M.D.
PHILADELPHIA

attempt will be made in this paper to enter discussion of the etiologic factors underlying gic pulmonary disease. Suffice it to say that monary allergy when present may be con- ed a part of the general systemic reaction. form of pulmonary allergy, whether the nt is sensitized to bacteria, pollen or food, is arily a medical problem, requiring individual tigation and consideration to determine the rlying cause.

the underlying cause can be found and ppriate treatment which will eliminate the se instituted, the problem is solved. How- as every one knows, the problem of allergy, mic or localized, does not lend itself to an solution, since one is not dealing with a dis- per se but with a syndrome, or a group of ptoms, present as a result of some underlying logic condition of the body. Pulmonary gy, or bronchial asthma, is no exception. In the differential diagnosis may disclose that o-called asthmatoid symptoms are not caused n allergic factor but are the result of organic nges in the tracheobronchial tree itself or in djacent structures. In the tracheobronchial any marked alteration of the normal contour he subglottic larynx, of the trachea or of bronchi may produce symptoms which simu- allergic asthma. Endotracheal or bronchial ths, a foreign body or thick secretion, for mple, may produce the characteristic wheeze ciated with such asthma. Organic changes rring in adjacent structures, such as the ence of a foreign body in the esophagus or rged mediastinal glands, thymus or other roaching structures may, by pressure on the heobronchial tree, produce the same effect. becomes apparent that Dr. Chevalier Jackson's horism, "All is not asthma that wheezes," uld be kept in mind in the treatment of hma.

From the Bronchoscopic Clinic, Graduate Hospital e University of Pennsylvania.

Thesis submitted to the Faculty of the Graduate ol of Medicine of the University of Pennsylvania rd the requirements for the degree of Master of ical Science [M.Sc. (Med.)] for graduate work in choscopy, in 1944.

BRONCHOSCOPIC AID

It is in these cases that the bronchoscopist may be of aid in the diagnosis and treatment of "bronchial asthma." As stated, true bronchial asthma is primarily a medical problem, and a competent internist should undertake proper studies to determine the causative factors. He may be aided by a competent and well trained bronchoscopist in several ways.

Whether the patient is an adult or a child, there is no substitute for direct inspection of the tracheobronchial tree when definite clinical symptoms are present. A preliminary roentgen examination should be carried out, but even in those cases in which this examination is reported to have yielded negative results one is justified in making a direct inspection of the air and food passages.

The value of bronchoscopy in the investigation of pulmonary disease is an accepted fact. It is the only method whereby the tracheobronchial tree can be surely and carefully examined. In the course of the examination one can observe the appearance of the mucous membrane and the caliber and contour of the trachea and of both main bronchi, searching for evidence of intrinsic growth or extrinsic compression, altering the size of the lumen. In addition, the general conformation of the openings of the bronchial branches to different lobes may be observed relative to the presence or the absence of organic changes, such as thickening, fixation and displacement. Likewise, the presence of abnormal tissue or secretions and other details may be noted in localizing and identifying abnormal changes. Bronchoscopy has certain limitations in that one is unable to see lesions distal to points of direct view, and in these cases additional valuable information may be obtained by the use of retrograde telescopic study through the bronchoscope and pneumonography.

While making the direct inspection, the collection of an uncontaminated specimen of secretion directly from the tracheobronchial tree for complete bacteriologic study is of extreme importance. With proper training and organization, bronchoscopy performed on a patient who is under local anesthesia is a safe procedure and

may be accomplished without undue discomfort to the patient. The small amount of discomfort associated with the instrumentation is more than offset by the valuable information obtained.

BRONCHOSCOPIC DIAGNOSIS AND TREATMENT OF CONDITIONS SIMULATING ASTHMA

Chevalier Jackson,[1] Gabriel Tucker,[2] L. H. Clerf [3] and others have repeatedly directed attention to the possibility that a foreign body may produce symptoms of asthma. This is true particularly in children, with whom a history of foreign body may be entirely unsuspected and the presence of foreign body not even considered. As a rule the child with symptoms suggesting asthma is treated for asthma for a variable period. Eventually, if the symptoms become definitely worse, he is hospitalized in desperation. After hospitalization, proper studies may reveal the foreign body or other changes within the air or the food passages. Competent roentgen studies will aid in establishing the diagnosis in the majority of these cases. In the bronchoscopic clinic with which I am associated we have a definite routine in the roentgen examination of these patients. We request anteroposterior and lateral projections of the neck, inspiration and expiration roentgenograms of the chest in both the anteroposterior and the lateral view, a careful fluoroscopic study with an opaque mixture, and roentgenograms of the swallowing function in every case.

TABLE 1.—*Bronchoscopic Observations on One Hundred and Seventy-Six Children Admitted to Hospitals Because of Symptoms Simulating Asthma, Which Did Not Readily Respond to Treatment with Epinephrine*

Nature of Involvement	Patients	Endoscopic Procedure
Retropharyngeal abscess	1	Incision and drainage
Foreign body in larynx	5	Direct laryngoscopy
Organic changes in larynx	8	Direct laryngoscopy
Tracheal compression	14	Bronchoscopy
Bronchial foreign body	13	Bronchoscopic removal
Esophageal foreign body	5	Esophagoscopy
True asthma, little secretion	47	Bronchoscopy for diagnosis and aspiration
True asthma, thick secretion	83	Bronchoscopy for diagnosis and aspiration
Total	176	

In a review of the records of 176 children admitted to the group of five different hospitals for bronchoscopic examination because of symptoms simulating asthma, which had not readily responded to the orthodox treatment, it was found that some interesting observations had been made. They are summarized in table 1.

Several outstanding illustrative cases from this group will be briefly summarized.

CASE 1.—E. S., a 13 month old white girl, was admitted to Abington Hospital on Aug. 11, 1941 because of persistent wheeze, occasional cough and paroxysmal dyspnea associated with marked intercostal retraction. The paroxysms of dyspnea would sometimes last several hours and then clear up; however, the wheezing was present at all times. The child had been treated at home for these "allergic" manifestations for almost two weeks because on previous occasions epinephrine had relieved the symptoms. For three to four days prior to admission she had become definitely more dyspneic and had continuous elevation of temperature. On her admission to the hospital, definite laryngeal stridor associated with considerable dyspnea and a loose cough, was noted. Because of the laryngeal stridor a lateral roentgenogram of the neck was requested in addition to the routine roentgen studies. This examination revealed a small safety pin in the larynx, the spring portion in the glottis and the point and keeper in upright position (fig. 1). Removal of the foreign body by direct laryngoscopy cured the "asthma." The child had the asthmatoid wheeze usually heard in cases of foreign body.

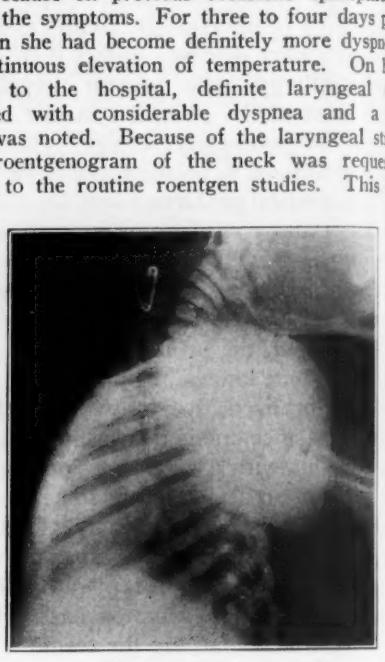


Fig. 1 (case 1).—Lateral (left side) view of the neck showing a safety pin in the larynx.

CASE 2.—P. K., a white girl aged 16 months, was brought into the receiving ward of Abington Hospital by the mother with a request that the child be given some epinephrine because she was having an "attack of asthma." On further investigation it was found that the parents and the child had been visiting relatives on a farm. While there, the child had been playing outdoors in one of the rooms when the mother suddenly heard her crying and coughing convulsively. The cough gradually subsided, but there was a loud wheeze. A physician was called who administered epinephrine according to the mother, with apparent relief of symptoms. While the parents were driving home from the farm the same evening, the child had a recurrence of wheezing so severe that they stopped at the hospital for further administration of epinephrine. The mother attributed the onset and entire sequence of symptoms to the musty, damp surroundings at the farm house.

1. Jackson, C.: Chronic Non-Specific Infections of the Lungs, J. A. M. A. **87**:729 (Sept. 4) 1926.

2. Tucker, G.: Bronchoscopy in Pulmonary Disease, Ann. Int. Med. **8**:444 (Oct.) 1934.

3. Clerf, L. H.: Present Status of Bronchoscopy in Bronchial Asthma, Ann. Int. Med. **9**:1050 (March) 1936.

sical examination indicated that the abnormal ion was limited to the middle and lower lobes of ght lung, with rales heard only on the right side. ntgen studies revealed a carpet tack in the right bronchus (fig. 2). The child apparently had ed the tack while playing on the floor. The time et of symptoms was definite, although the actual t was unsuspected. The child was admitted to spital, and the tack was removed bronchoscopically me evening. The wheeze ceased, and the child mained symptom free.

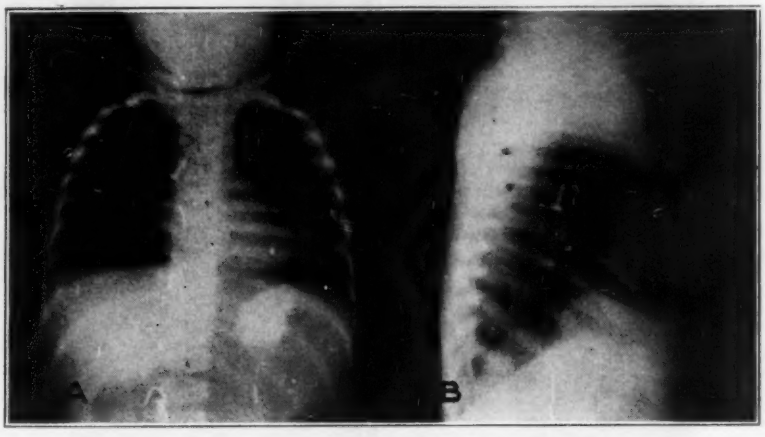
E 3.—The following case is interesting because of culiar circumstances:

H., a white boy aged 5 years, was admitted to ton Hospital, Sept. 6, 1940, because of high fever, ent cough and loss of weight. The mother eered the information that "the child had always weak chest and had had occasional cough since nths of age," at which time he was supposed to had pneumonia. He was susceptible to frequent and during these colds had what she termed

found to be a small fragment of peanut. Subsequently bronchoscopy was performed three times for aspiration and treatment of the infection in the middle and lower lobe of the right lung. The lung cleared, and the patient recovered completely. He finally admitted that he had eaten some peanuts and, through fear of being detected, had gulped them down and choked. The incident corresponded to the onset of symptoms six weeks before. This case illustrates the point that proof of allergy does not exclude the presence of a foreign body.

CASE 4.—This case demonstrates that foreign bodies outside of the respiratory tract may produce symptoms simulating asthma.

K. S., An 8 week old boy, was admitted to Abington Hospital on April 24, 1941, with a history of having a deep cough with a harsh voice when he cried, and shortness of breath, of four weeks' duration. The symptoms had become progressively worse, so that at the time of admission the baby had become very dyspneic and sometimes cyanotic during feedings. It had also been noted that he regurgitated large amounts of his



g 2 (case 2).—*A*, anteroposterior and, *B*, lateral (right side) view of the chest, showing a carpet tack right main bronchus.

ness in the chest" and often "purred like a cat." d been tested, and she claimed he was sensitive to dust and certain foods and was particularly ve to peanuts. For this reason he had been for- to eat peanuts. The present illness began five before admission to the hospital. There was a history that at this time the parents had caught ating peanuts. The child denied the charge. One emained certain: His condition had become pro- vely worse since that time. A roentgen examina- f the chest, requested by the family physician two after the onset of the symptoms, was reported owing no abnormality. Epinephrine did not etely relieve the dyspnea or the wheezing.

physical examination there appeared to be definite es in the middle and lower lobes of the right lung. oentgen examination showed increased density of tire middle lobe and lesser changes in the lower The bronchoscopic examination revealed a hemor- inflammatory reaction of the entire trachea and right main bronchus, with considerable granula- issue present in the orifice of the middle lobe nus. The lumen of the right middle lobe bron- appeared occluded by the inflammatory exu- A side curve forceps was passed through the noscope into the bronchial orifice, and on closing rceps a firm substance was felt. The object was

feedings. The mother attributed the difficulties to a cold which the baby contracted several weeks after he was brought home from the hospital. She casually stated that there was a daughter 3 years of age who

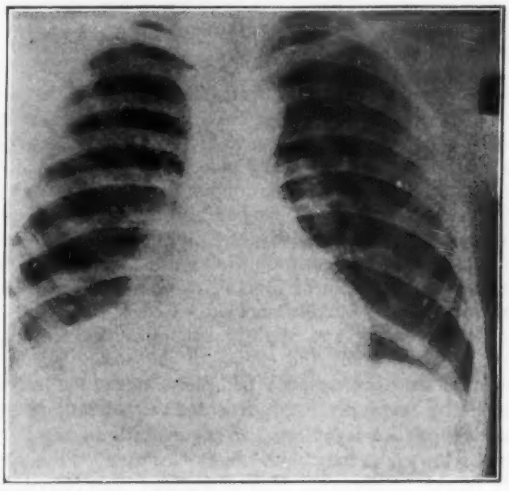


Fig. 3 (case 3).—Roentgenogram of the chest of a boy who had a fragment of peanut removed from the middle lobe of the right lung.

told her that she fed the baby something to keep it quiet. The mother did not attach any importance to this. She consulted the family physician, who thought that the infant had a cold and also that it might be sensitive to something. However, when the child became definitely worse, he suggested hospitalization.

On admission the patient had a definite inspiratory and expiratory wheeze, with a deep, barking cough. When quiet, it did not appear dyspneic, but the wheeze was constantly present. Routine roentgen examination revealed the chest to be clear, but in a lateral roentgenogram the posterior wall of the upper part of the trachea was displaced forward by an opaque foreign body that appeared to be a button. A test of swallowing function with liquid barium sulfate showed that very little of the opaque substance passed beyond the foreign body (fig. 4).

some beef soup one evening when she thoug choked on a bone. She had marked pain on swal for about three days, after which time the pa appeared. However, she had noted that from th on she began to cough considerably more, the being particularly severe at night while she wa down.

Because of this history and the roentgen fi bronchoscopic examination was performed. This nation, made after the patient had become compe revealed considerable granulation tissue in the main bronchus. It showed the presence of an irr shadow suggestive of a foreign body. With a self-expanding forceps, the object was grasp removed. It proved to be a large piece of bee which had been there for at least two months, co ing the patient's statement of choking.

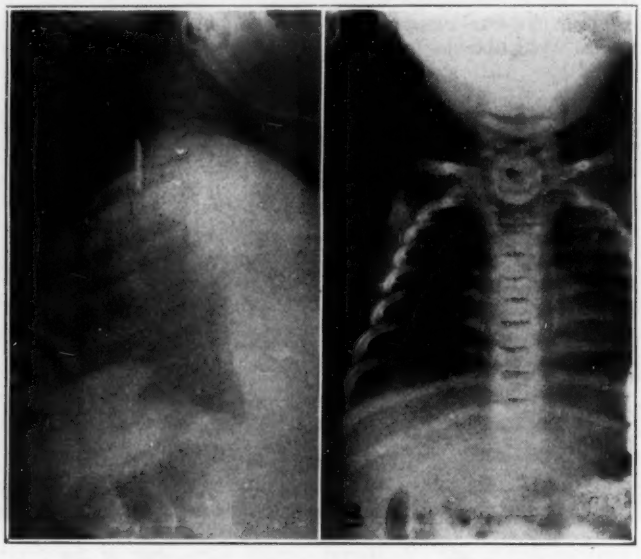


Fig. 4 (case 4).—Roentgenograms showing a button in the esophagus.

On esophagoscopic examination the foreign body was at first difficult to visualize because of the ulceration of the esophageal mucous membrane and the granulation tissue around it. It was located and grasped with a Mathieu forceps and removed. The symptoms completely disappeared after the esophagoscopic removal of the button from the esophagus.

CASE 5.—This case illustrates the fact that the confusion in diagnosis is not limited to children alone:

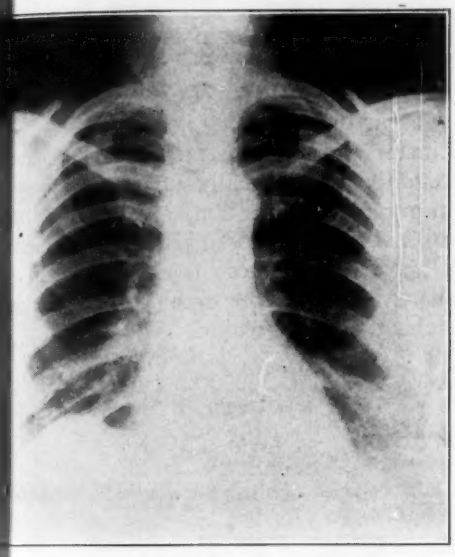
M. F., a white woman aged 58, was admitted to the hospital of the Protestant Episcopal Church, Oct. 14, 1941, with a history of continuous distressing cough of eight weeks' duration. She had chronic cardiac disease and had been admitted to the hospital several times because of decompensation. On this admission she presented all the clinical signs of marked cardiac decompensation. Both ankles showed extensive edema, and she was dyspneic and slightly cyanotic. Several days after hospitalization, the edema of the ankles began to disappear and the dyspnea definitely improved, but the distressing cough persisted. Roentgen examination of the chest revealed a large area of pneumonitis in the lower lobe of the right lung with slight elevation of the right side of the diaphragm. These findings were attributed to the cardiac disease. In the course of taking the history the resident elicited the fact that about two months prior to the present admission the patient had been eating

CHARACTERISTIC BRONCHOSCOPIC FINDI IN ALLERGIC PULMONARY DISEASE

Often one hears the classic description o blanched appearance of the mucous memb and the presence of thick, sticky secretion, w are stated to be always associated with ast My observations in a large number of cas asthma have not confirmed this. I have associated with Dr. Gabriel Tucker for the nine years, and during this period many pat have been referred to his clinics from the all departments of the Graduate Hospital of University of Pennsylvania and the Hospit the University of Pennsylvania. In additio large number of patients have been referre my clinics in several other hospitals, and fundamental knowledge gained from the bron scopic observations of at least a thousand of t patients is that no fixed picture is characte of any patient. By this I mean that the s person may present entirely different change different observations, depending on whether

nation is made while the patient is suffering an acute attack or at a short or a long al after an attack. In each period the find- may be entirely different. The circum- that the patient is suffering from an infec- f the upper respiratory tract may be suf- to alter the appearance of the entire al pattern of the tracheobronchial tree.

studies of Van Loon and Diamond [4] con- th our observation that this is particularly f children. We have noted that in many



5 (case 5).—Except for elevation of the dia- on the right side, there is little to suggest the ce of a foreign body.

nces a child examined at long intervals after ttack may present a practically normal rance, the mucous membrane being smooth elvety, with absence of inflammatory reac- or expiratory collapse of the posterior al wall.

the other hand, in all patients examined g an attack, whether children or adults, hanges are fairly constant and uniform: mucous membrane is always hemorrhagic, nd redundant, greatly reducing the caliber e lumen of the trachea and both main hi. Secretions are always present and so ous that they are difficult to aspirate. The phenomenon of collapse of the posterior al wall, described by Lukens [5] and Moore,[6] is frequently present in children and almost always present in adults during status asthmaticus.

Clerf,[7] in his early paper on this subject, confirmed the observation of Lukens and Moore, and described in detail the physiologic changes in the lumen of the normal trachea and bronchi during respiration. Briefly, during inspiration the lumen attains its largest diameter, while on expiration the tendency is for the lumen to become uniformly smaller. In acute asthma there is marked deviation from this normal phenomenon. In 102 cases in which bronchoscopy was performed during status asthmaticus, certain definite clinical findings were recorded. During such attacks every patient showed a marked hemorrhagic and edematous appearance of the mucous membrane of the trachea and both main bronchi. In many patients this inflammatory process was so marked that the caliber of the lumen was reduced to almost one half of the normal size. On expiration there was collapse of the posterior wall, completely obliterating the tracheobronchial lumen, with a crescent-like appearance being produced by the bulging of the mucous membrane against the fixed concavity of the anterior wall (fig. 6).

Add to this the presence of thick, tenacious secretion, and one readily understands why these patients undergo such acute respiratory em-

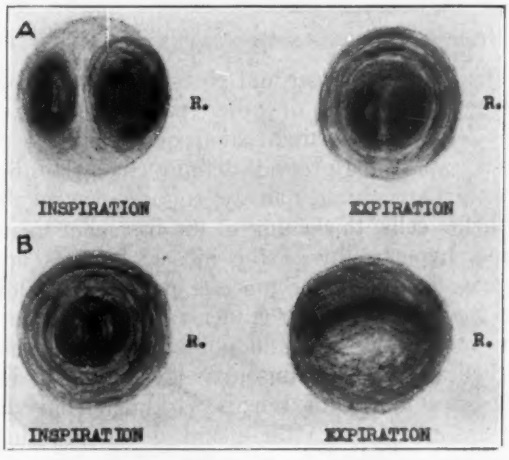


Fig. 6.—Diagrammatic representation of the changes in caliber of the tracheal lumen during the respiratory phase in a normal state of health (*A*) and in status asthmaticus (*B*).

barrassment. Relative to this phase, several interesting manifestations have been noted. In some patients, though the secretions are thick and tenacious, they maintain a fluid consistency, and on inspiration the air appears to exert a

Van Loon, E. L., and Diamond, S.: Broncho- Aspect of Asthma in Children, Am. J. Dis. **63**:217 (Feb.) 1942.

Lukens, R. M.: Bronchoscopy in the Treatment ma, Laryngoscope **35**:227 (March) 1925.

Moore, W. H.: Ciliary Inhibition or Destruc- Bronchial Asthma, Am. J. M. Sc. **169**:799 1929.

7. Clerf, L. H.: Bronchoscopy as an Aid in the Diagnosis and Treatment of Bronchial Asthma, J. A. M. A. **89**:872 (Sept. 10) 1927.

centrifugal force, opening a central canal, thereby forcing the secretion against the wall. Thus, it may be surmised that in the smaller bronchioles, where this no longer can occur, the inspired air does not have ready access to the alveolar spaces. Another peculiarity has been noted in patients who do not have this type of secretion but have discrete flecks of thick mucus, which cling to the wall of the trachea and bronchi. Because of the tenacious character of the mucus, it is difficult to expectorate and even offers resistance to bronchoscopic aspiration. In both these types a definite problem is created by the collapse of the posterior wall, because it hinders the adequate expectoration of the secretion. Here the process resembles more ameboid movement except that it has the boomerang effect of forcing the secretions not only out toward the larynx but also in the opposite direction into the smaller bronchi. Thus it becomes apparent that the persistence of this process increases the amount of retained secretions and adds considerably to the respiratory distress of the patient (fig. 7).

complete occlusion of the many bronchi e the danger in the use of narcotics and atr which abolish the cough reflex and thicke secretion, thus making it more difficu cough up.

Further, the increase in the thickening lining membranes of the bronchus interfere the flow of both arterial and venous blood a the same time affects the sensitivity of the endings. This interference with blood flo with the passage of nerve impulses may in explain some of the difficulty of obtaining in asthmatic patients during an acute a These marked histologic changes are no quently present in children, and this may explain the infrequency of marked status maticus in them (fig. 8).

Eiman [9] has demonstrated that the re secretion may eventually undergo change form organized fibrin plugs, which take the of casts of the surrounding bronchial lumen also showed that these fibrin casts had e resiliency and were capable of conside stretching before breaking.

Fig. 7.—Lateral view of the trachea (diagrammatic). Note how collapse of the posterior wall in statu maticus hinders expectoration of secretion.

PATHOLOGIC CHANGES IN STATUS ASTHMATICUS

The work of Huber and Koessler [8] and subsequent observations of other pathologists have definitely demonstrated that frequent and severe attacks of asthma produce definite changes in the bronchial structures, namely, engorgement of the epithelial cells, thickening of the basement membrane, hypertrophy of the muscle bundles and increase in size of the mucous glands. In addition there is marked prominence of the lymphoid connective tissue and esinophilic cells in the subepithelial and extramuscular layers. The increased amounts of mucus exuding from the mucous glands into the gland ducts and then into the lumens of the bronchi and the stronger contraction of the hypertrophied muscle bundles, combined with the actual increase in the thickness of the wall, act simultaneously to produce greater pressure on the bronchial wall. At the same time, many of the smaller bronchi are occluded completely by this sticky, tenacious mucus that is produced in such large quantities that the passage of air into the alveolar spaces is stopped. The overproduction of mucus and the

All these observations were consistently out in varying degrees in the postmortem o vations of 3 cases reported by Meranze.[10]

BRONCHOSCOPY IN THE TREATMENT OF ASTHMA

I wish to reiterate here that any for allergy is primarily a medical problem. patient should be treated first from that a That bronchoscopy has been of inestimable in the treatment of bronchial asthma is a cepted fact. The value of direct inspection tracheobronchial tree and that of eliminati foreign body and other factors which would rise to symptoms that might be misinterp as those of asthma have already been discuss detail.

Little has been said concerning the colle of an uncontaminated specimen of secre under sterile conditions, directly from the b chial source. This specimen, when pro examined by the laboratory, will reveal the

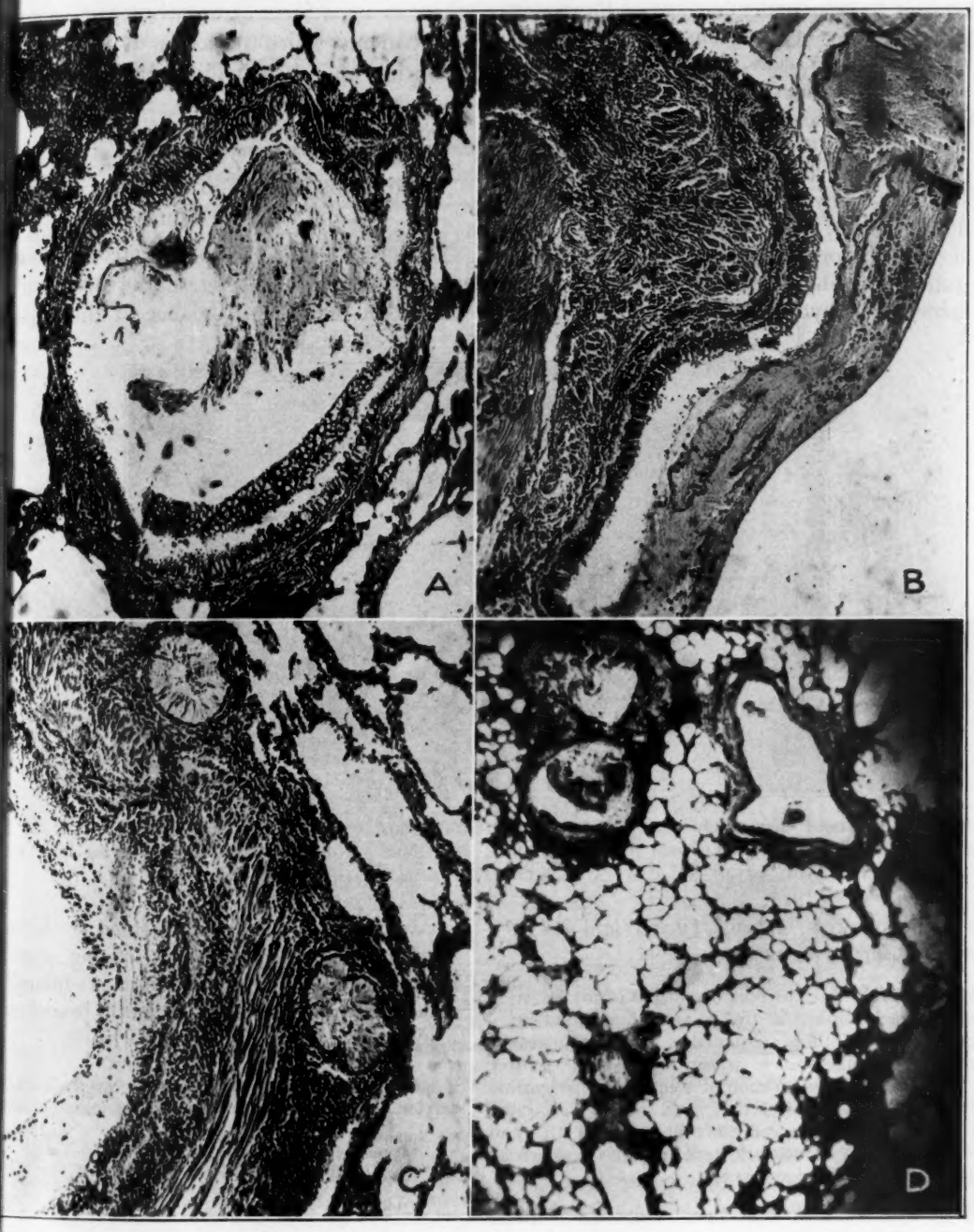
8. Huber, H. L., and Koessler, K. K.: Pathology of Bronchial Asthma, Arch. Int. Med. **20**:689 (Dec.) 1922.

9. Eiman, J.: Postmortem Observations on S Asthmaticus, Abington Hospital, Philadelphia.

10. Meranze, D. R.: Postmortem Observatio Three Cases of Status Asthmaticus, Mount Sinai pital, Philadelphia.

ganisms present. Today, with the use of otherapy, it is extremely important that one tain the type of organisms present, so that proper sulfonamide compound may be ad- tered. Clinical observations made in the results. The details of this work will be published in another paper.

The value of autogenous vaccine when properly administered, particularly in children, has been shown by the work of Crump.[11]



ig. 8.—*A*, cross section of a large bronchus with thick secretion filling the lumen. *B*, cross section of a chial wall showing hypertrophy of muscle bundles and the presence of thick, organized fibrin close to the elial layer. *C*, mucous glands (two) in the wall of a normal bronchus. *D*, mucous glands in a bronchial in status asthmaticus. The prominence of these glands as compared with the normal is to be noted.

year have shown that these drugs may be inistered bronchoscopically directly into the heobronchial tree, with unusually effective

11. Crump, J.: Asthma in Children Treated with Autogenous (Bronchoscopic) Vaccine, Am. J. Dis. Child. **58**:768 (Oct.) 1939.

The vaccine per se may not have any desensitizing effect on the patient unless the allergy should be caused by a specific bacterium which is present. However, in the majority of the cases it serves to immunize the patient against the organisms which he harbors and renders him less susceptible to recurrent infections of the respiratory tract. Our observations have shown that in at least 65 per cent of our patients attacks of status asthmaticus were preceded by acute infections of the respiratory tract. The roentgen examination of the chest during this phase revealed marked accentuation of the hilar markings and, in many cases, even of the mediastinal shadow (fig. 9).

Of great importance during the bronchoscopic aspiration is the hypodermic injection of solution of epinephrine hydrochloride made just before the bronchoscopy. Gabriel Tucker and Richard Kern [12] observed that:

> After careful bronchoscopic aspiration of all secretion from the tracheobronchial tree of an asthmatic patient, a large quantity of thick, obstructive secretion appeared in the trachea and bronchi within a few minutes after the hypodermic administration of solution of epinephrine hydrochloride. The secretion was readily aspirated and the patient experienced more prompt, effective and permanent relief of the attack than had been experienced without the use of epinephrine.

This observation has been confirmed many times, so that at present administering epinephrine just prior to bronchoscopic aspiration in cases of asthma has become a routine procedure. The subsequent report of Brown [13] on the intravenous use of theophylline ethylenediamine served to establish another useful adjunct. results of the injection of this drug are eq effective, with the advantage of prolonged tion of the therapeutic effect.

These findings tend to confirm the belief there is some form of bronchospasm in ma the patients which responds to the use of nephrine and theophylline ethylenediamine though many observers do not concur in opinion.

BRONCHOSCOPY IN THE TREATMENT OF STATUS ASTHMATICUS

A series of 102 patients treated by bronc copy during attacks of status asthmaticu shown in table 2. A glance at this table

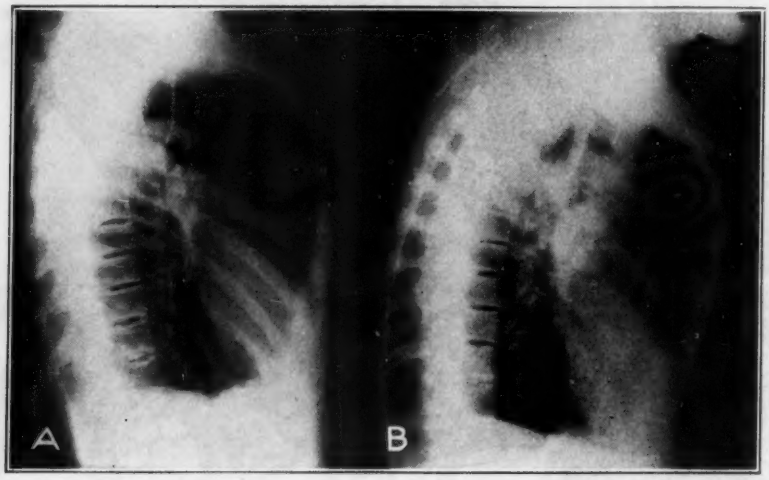


Fig. 9.—*A*, lateral view of the chest of an asthmatic patient during an interval free from attacks. *B*, l view of the chest of the same patient during an attack of asthma. Note the accentuation of the hilar sh with increase in density of all the structures in this region.

reveal that 1 patient was treated by bronc copy twelve different times during severe tacks. This patient was almost immedia relieved of symptoms after each bronchos aspiration.

TABLE 2.—*Bronchoscopic Aid in Status Asthm*

Number of Patients in Treatment Group	Bronchoscopic Aspirations per Patient	Total	Mortal
1	12	12	
6	8	48	
1	7	7	
4	6	24	
1	5	5	
10	4	40	
16	3	48	One patient
22	2	44	half hour a
41	1	41	bronchoscop
102		269	

The series runs back over a period of s years, and 269 bronchoscopic examinations

12. Tucker, G., and Kern, R.: Personal communication to the author.

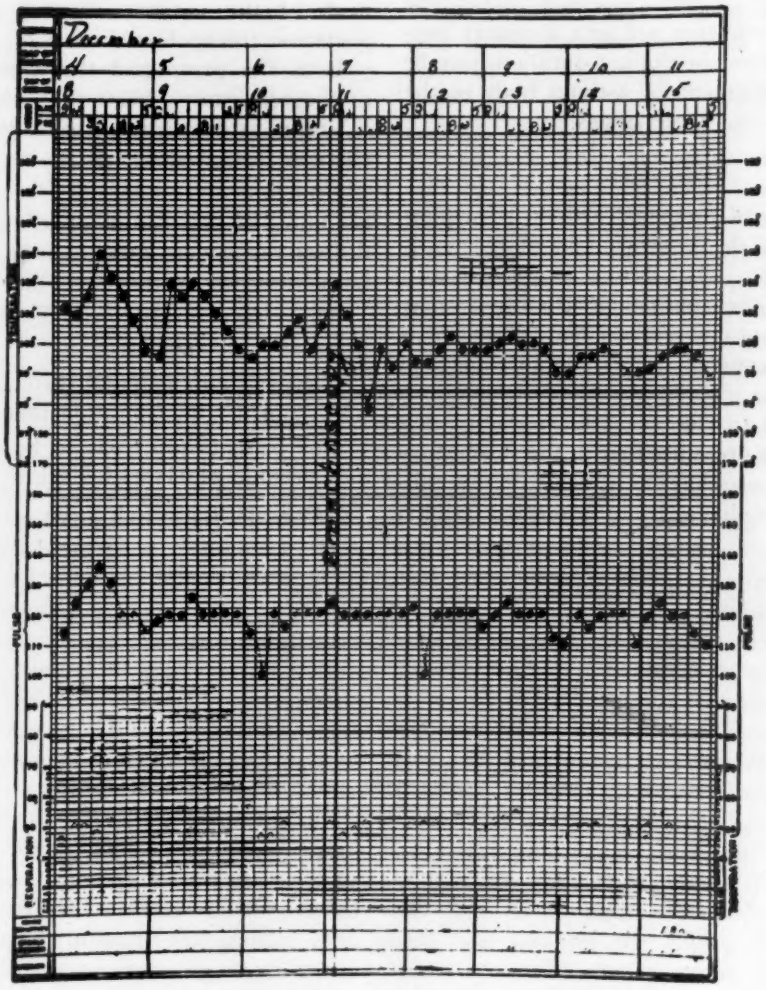
13. Brown, G. T.: Aminophyllin in Asthma, J. Allergy **10**:64 (Nov.) 1938.

rations have been performed on the 102
nts.

single mortality in this series deserves brief
nation. The patient had undergone bronchoscopic
ination and treatment twice previously, with defi-
relief of symptoms. He left the hospital and was
en again until about six weeks later, when he was
itted to another hospital. A bronchoscopic con-
ion was requested at this time, and bronchoscopy
recommended in view of the previous relief. The
hoscopic examination, however, was deferred by
ttending physician for another period of three

Despite the fact that the secretions had just been aspirated, all the smaller bronchi and bronchioles were occluded by organized plugs of mucus that could be stretched like a rubber band. To have helped this patient, the bronchoscopic aspiration should have been carried out when it was first recommended, and not four weeks later.

In all cases, during the bronchoscopic examination oxygen was administered through an attachment on the bronchoscope, thereby relieving the dyspnea.



ig. 10.—Temperature chart of a patient who had been in status asthmaticus for three days. Bronchoscopic ration not only completely relieved the asthma but caused the patient's temperature to drop.

ks, during which the patient was in almost constant
e asthmatic attacks. At this time he was unable
ough up any secretion, and, as a last resort, bron-
copy was undertaken. The bronchoscopic examination
aled that the trachea and both the right and the
main bronchus were completely filled with ge-
ous, sticky secretions, of which at least 4 ounces
cc.) was aspirated. Immediately after the bron-
copic procedure the patient seemed considerably
ved. He was being returned to the ward when he
denly collapsed and stopped breathing. The post-
tem examination revealed advanced pulmonary and
eralized systemic changes.

Since many of the patients during attacks were too sick to be moved, the bedside bronchoscopic technic of Gabriel Tucker has been used with the majority of them:

The bedside bronchoscopic technic was first used in the treatment of postoperative pulmonary complications. The patient is not removed from the bed. The bronchoscopic setup is taken to the bedside, or the patient may be brought to the operating room in his bed. The head of the bed is elevated to an angle of about 30 degrees, and the recumbent patient is placed diagonally across the bed so that his head comes over the edge of the bed.

The bronchoscope is introduced, oxygen is given through the bronchoscope, and examination and aspiration are carried out [with the patient] in this position.

In routine examination of patients not in acute distress, the usual bronchoscopic table is used.

Of utmost importance in the treatment of patients subject to asthmatic attacks, if the greatest relief is to be obtained, is that they be given the treatment as soon as possible during an attack, whether it is in the middle of the night or during the day.

Understanding of the associated pathologic changes in this condition will give a clearer conception of why bronchoscopic aspiration may be of aid in the treatment of asthma both in the quiescent and in the acute stages.

SUMMARY

The treatment of bronchial asthma is primarily a function of the internist and more specifically the allergist.

Since many other pathologic conditions may produce the symptoms of bronchial asthma, it is extremely important that these factors be kept in mind.

It is essential to rule out the possibility that a foreign body is present either in the respiratory tract or in the esophagus, particularly in children, before the diagnosis of bronchial asthma is made. In a series of 176 children obser bronchoscopically because they presented sy toms of asthma, 18 had foreign bodies in respiratory tract, 5 had such objects in the eso agus and 23 had other organic changes.

The majority of the patients in status a maticus who were observed bronchoscopic showed a marked hemorrhagic and edema appearance of the mucous membrane of trachea and both main bronchi, with the pr ence of thick, tenacious secretion. In addi most of the patients showed collapse of posterior tracheobronchial wall.

Both the gross and the microscopic stu of the respiratory tracts of 5 patients who d in status asthmaticus revealed the characteri changes described.

Bronchoscopic aspiration of the pulmon secretion of patients in status asthmaticus w do not respond to medical treatment may of be a lifesaving measure.

The results in 102 patients treated bronc scopically are tabulated.

Oxygen administered through the bronc scope during the aspiration relieves the dyspn

For patients too toxic to be moved, the b side technic of Gabriel Tucker should be us

255 South Seventeenth Street.

CLINICAL RESULTS IN PATIENTS TREATED BY INTRANASAL ETHMOIDECTOMY

FRED W. DIXON, M.D.
CLEVELAND

The evaluation of any surgical procedure depends on the degree of comfort afforded those treated on and the length of time this benefit endures. The comfort of the patient following surgical operation on the sinuses is in proportion to his freedom from headache, his ability to breathe through his nose, the reduction of postnasal discharge and the nonrecurrence of the polyps. That these results have not usually been achieved has caused a tendency in some medical circles and among the laity to depreciate all forms of surgical treatment of the sinuses.

It is the duty of the rhinologist to correct this impression. I believe that failure to achieve the results expected is due to four main causes: (1) ill advised attempts by those not qualified to perform this type of surgical operation, (2) incomplete removal of pathologic tissue by those unqualified, (3) uncontrolled allergy and (4) inadequate postoperative care.

The degenerated ethmoid labyrinth with its polypoid formations is a common sight in the rhinologist's office. In my search in the dissecting room over a period of many years polyps have frequently been encountered in the ethmoid cells, less frequently in the maxillary sinus, and while one occasionally finds thickened mucosa in the frontal sinus and the sphenoid sinus, rarely is it polypoid in nature. In the nasal passage itself, while polyps may spring from any mucous surface, the nasal septum, the floor of the nose, the inferior turbinate and the medial wall of the superior turbinate are usually free. The polyps usually spring from the edges of the ostiums of the anterior and posterior ethmoid cells. Sometimes polyps occurring in the maxillary sinuses may tumble through the ostiums into the nasal passages.

These polyps, because of their location, interfere with the ventilation and the drainage of the frontal, the maxillary and the sphenoid sinuses. It is obvious that if one could unlock the sinuses before their mucosa has become irreversibly changed, no further operation would be necessary. To remove the polyps alone is surgically inadequate. To remove the isolated cells in the ethmoid labyrinth is impossible because of their arrangement. I make this statement with due regard to the roentgenogram and the displacement technic.

In conversation with other rhinologists I find my experience coincides with theirs in that though one earnestly desires to control allergy, the problem of doing it is still a perplexing one. The difficulty of demonstrating the allergen, the change of allergen from year to year, the long course of treatment required and the recurrence of allergy often make persuasion to accept allergic investigation difficult. However, a careful history will often furnish the answer. This should be taken from all allergic patients. Many will need no further investigation.

Now, given a patient with a nasal cavity filled with polyps, what steps should be taken to restore this patient to as nearly normal a condition as possible and maintain him in this state? No claims are made that a nose once affected will ever return to normal, but one can make the patient comfortable and he will be satisfied with his surgical treatment. I feel that a thorough opening of the ethmoid labyrinth with the subsequent ventilation and drainage of other sinuses which that makes possible offers the best solution. Whether one accomplishes it by the intranasal route, the external approach or the transantral method depends on experience and skill and on the choice of the operator. Thoroughness is the important factor. I prefer the intranasal approach. In my hands it has been satisfactory. It leaves no external scar or deformity, there have been no complications, and it has been adequate. Regardless of the type of approach, there are three landmarks for caution: the orbital plate, the fovea ethmoidalis and the cribriform plate. The first two are to be cleansed carefully; the third is to be avoided. A curtain of mucosa and submucosa is left to divide the fovea ethmoidalis and the cribriform plate. This is finally bent outward in order that the inspired air may better contact the olfactory area. The sense of smell may return.

Read before the Eastern Section of the American Laryngological, Rhinological and Otological Society, Philadelphia, Jan. 12, 1945.

This operation is done with the patient under local anesthesia. Irrespective of the operative approach, it is impossible to remove all cells. However, careful search for and thorough removal of all pathologic tissue are requisite for success. The swab, the suction tube and the probe are as essential as the punch forceps.

Recently there have entered the postoperative treatment of this condition two forms of therapy which are a great help, namely, those concerned

Lately it has been the custom at the ti operation to determine the type of orga Most of the cultures have shown growths staphylococcus or of mixed organisms respond to penicillin. After painstaking re of the ethmoid labyrinth, the patient is k the hospital for five days. During this 2 cc. of penicillin is given intramuscularly four hours, i. e., 120,000 units per day, total of 600,000 units. At the end of this

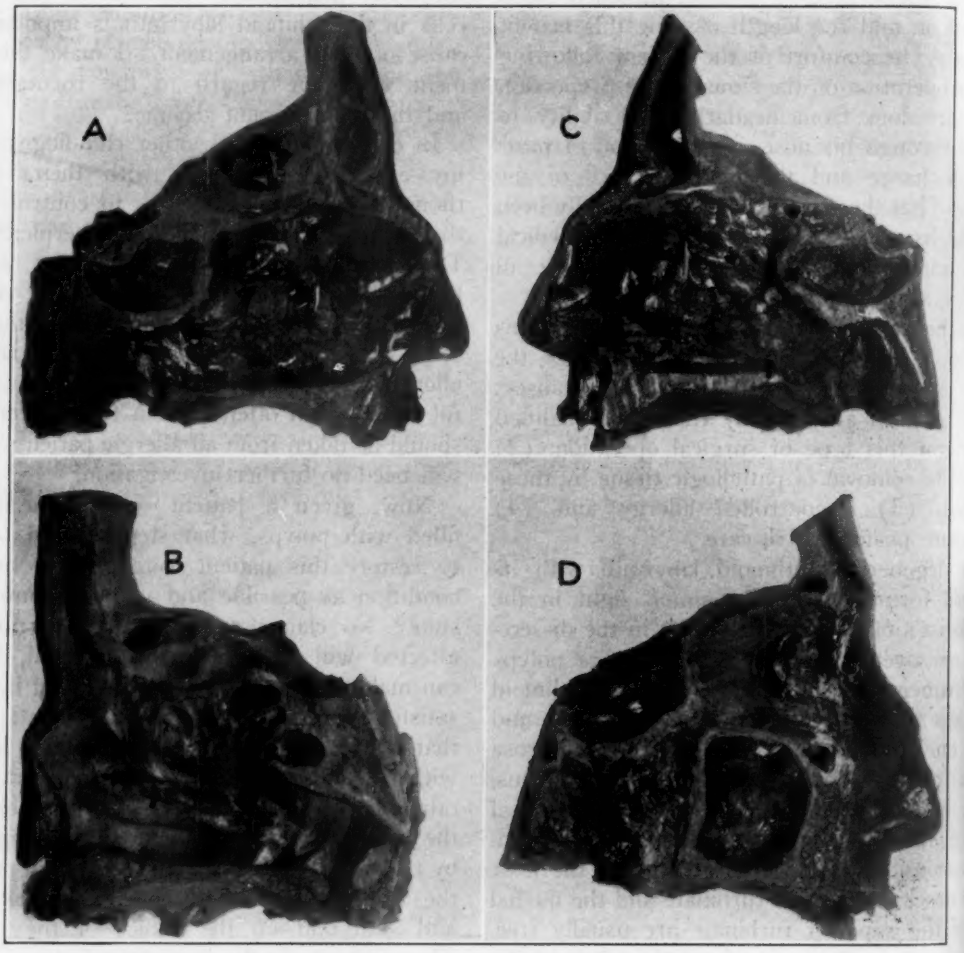


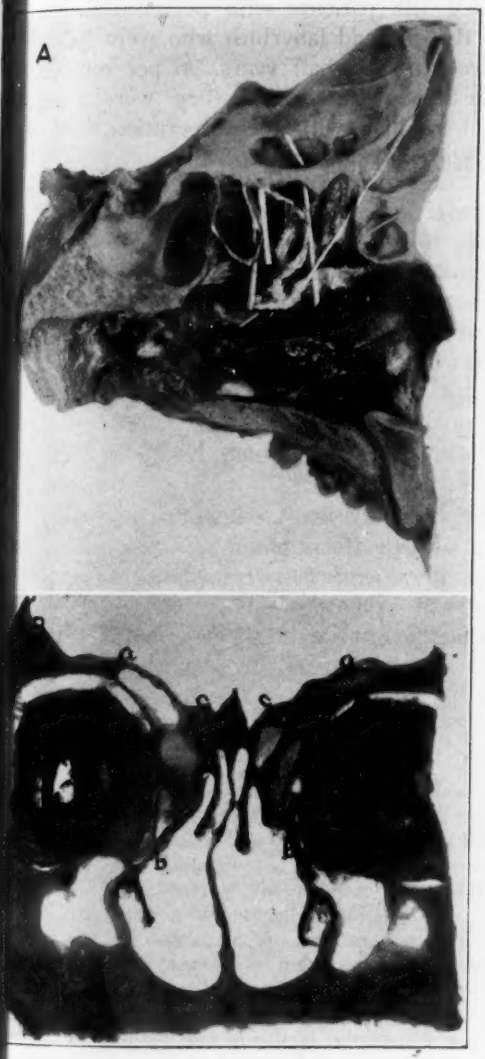
Fig. 1.—*A,* polyps hanging from the ostiums of the frontal and the ethmoid sinus. This finding doe require radical operation. *B,* polyps springing from the ostiums of all the ethmoid cells, requiring thorough o tion. *C,* polyps originating in the middle meatus. None is attached to the inferior turbinate or the medial s of the superior or the middle turbinate. *D,* the maxillary sinus of the patient whose middle meatus is seen There is a thickened mucosal lining, but only two small polyps are present.

with penicillin and sulfadiazine. They in no way replace surgical treatment, but as adjuncts they offer much help. If the sinal cavities have been well opened, the necrotic tissue largely removed, ventilation and drainage established, penicillin or sulfadiazine then given controls the infection. The area of operation heals more quickly by the lessening of the granulation tissue and of the recurrence of polyps.

the nose is usually dry. A heavy brown cr the area of operation can then be removed, the patient is discharged from the hospital. visits the office twice a week for one m Any recurring granulation tissue or poly removed in the office at the end of that He returns to the office each month for the three months. After that he is reexamined e six months or once a year as indicated.

is any recurrence of polyps, their removal office procedure to be done at the time of visit. Usually the frontal and the sphenoid es require no further treatment than that ribed. The maxillary sinuses may require ation or, if severely affected, further sur- treatment.

he most successful operation will end with ooth surface covering the orbital plate and



g. 2.—*A*, complex arrangement of cells making ologic diagnosis difficult. *B*, orbital plate and fovea oidalis (*ac* and *ab*) carefully cleansed. The cribri- plate (*cc*) has not been disturbed.

fovea ethmoidalis. The pathologist's report sections taken from the regenerated mucosa he area of the fovea ethmoidalis is as follows: e mucous membrane was covered by pseudo- tified columnar epithelium. In some areas were identified. There was an increased nber of enlarged cells containing vacuoles, namely, goblet cells containing mucin. The nuclei were vesicular and contained an average amount of chromatin material. The basement membrane was somewhat thickened and had a deep pink appearance. The underlying tissue contained many blood vessels, and in addition there were glands, predominantly of the mucous type." This report probably explains the normal clinical appearance of the mucosa in this area and its lack of dryness.

ANALYSIS OF RESULTS

A patient with a single polyp or a small number of polyps does not need a radical exenteration of all cells. Such patients were not included in this investigation. For this study I selected only those who were most difficult to manage, whose entire nasal cavity was filled, unilaterally or bilaterally, with polyps. This survey was made on 125 private patients. The only criterion used was my ability to follow them over a considerable period. This varied from one to twenty years. The average length of time was three and one-half years. There were 46 female and 79 male patients. The age ranged from 14 to 70 years. The average age of the female patients was 40 years and that of the male patients 42 years. Thirty-three had unilateral and 92 bilateral involvement. Fifteen patients had a submucous resection of the nasal septum done at the same time. This I found to be essential to obtain a proper view of the operative field. Twenty-eight had been operated on previously; 6 had systolic blood pressure over 200; 1 bled, requiring hospitalization five days after operation; 1 died three months and 1 six months later from intracranial hemorrhage. In the other 4 patients the blood pressure was reduced, since they were able to sleep normally in a prone position.

The complications of meningitis, thrombosis of the cavernous sinus, discoloration about the orbit and others mentioned in the literature have not been encountered. Two patients had postoperative headaches that persisted for one month, and a third has had an intermittent headache over a period of years that has defied all investigation.

Clinically, 30 of these patients were postoperatively allergic. Only 5 had ever been under the care of an allergist. Several were sensitive to tobacco and alcohol and were relieved on abstinence. Two worked in paints and were sensitive to varnishes. Several suffered only on having the body chilled on rising in the morning or had a physical type of allergy.

Postoperatively, 16 patients complained of a postnasal discharge, especially noticeable on the

advent of an acute infection of the upper respiratory tract, while 95 thought that they had no more colds than the average. None complained of any dryness in the throat. Three had moderate crusting in the nose, due to chronic maxillary sinusitis, but refused surgical treatment. Three had a persistent cough. All were able to breathe through the nose. Even those who were allergic usually had one nostril patent.

Recurrences.—There was no recurrence in 91 patients followed on an average of three years and six months. Thirty-four who had a recurrence were followed on an average of five years. These averaged two operations each in that period.

Satisfaction with Results.—When ques as to the results, 118 patients stated that were completely satisfied and 5 that they moderately well satisfied. Two were not fied; they had no recurrence of their p but their allergy could not be controlled. 5 moderately well satisfied patients, 2 we had been under allergic treatment without

SUMMARY

Of 125 patients with polypoid degener of the ethmoid labyrinth who were follow three and one-half years, 96 per cent on questioned stated that they were comfor and satisfied with their operation.

1207 Rose Building.

A MODIFICATION OF THE EXTRALARYNGEAL APPROACH TO ARYTENOIDECTOMY FOR BILATERAL ABDUCTOR PARALYSIS

DE GRAAF WOODMAN, M.D.
NEW YORK

This is a preliminary report of a modification the extralaryngeal approach to arytenoidecmy for bilateral abductor paralysis.

While I was in charge of the service in the d for patients with diseases of the ears, the e and the throat at the Presbyterian Hospital 1944, a patient with bilateral abductor paralu came to the ward. When this patient was g discussed with the chief of service, the sugtion was made that the external approach terior to the thyroid cartilage be tried rather n making a window through the thyroid tilage as described by Kelly[1] or removing posterior half of the cartilage as described Orton.[2]

The procedure to be described was tried. The rative technic was found relatively easy and result so satisfactory that this preliminary ort is presented. The procedure has been owed in other cases by other surgeons on our vice, and the cases will be reported as soon a series has been obtained.

PROCEDURE

a preliminary tracheotomy has not been done, the ent is prepared under local anesthesia for the placet of a semirigid woven silk intratracheal tube (under dance of the laryngoscope). A tracheotomy should be done before starting the operation. Intravenous duction of anesthesia has proved satisfactory.

n incision is made along the anterior border of the nocleidomastoid muscle at the level of the upper e of the thyroid cartilage and is carried down to the l of the cricoid cartilage (fig. 1).

he sternocleidomastoid muscle is retracted, exposing posterior edge of the lateral thyroid cartilage, with thyrohyoid muscle anterior to its posterior edge and inferior pharyngeal constrictor muscle attached to its posterior edge and to the inferior cornu. The attachment of the inferior cornu to the cricoid cartilage is a key landmark.

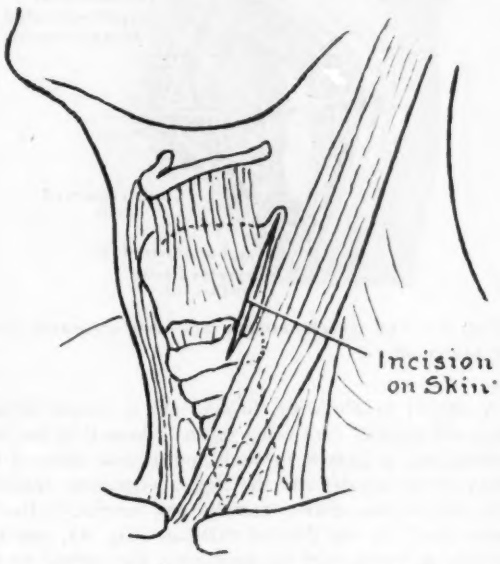


Fig. 1.—Placement of the cutaneous incision.

A vertical incision is made along the posterior edge of the lateral thyroid cartilage and the inferior cornu down to and through the perichondrium (fig. 2). The inferior constrictor is separated posteriorly; the cartilage is hugged closely and the perichondrium elevated around

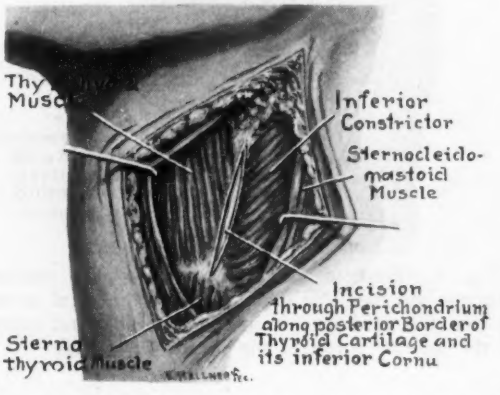


Fig. 2.—An incision has been made along the posterior border of the lateral thyroid cartilage and the inferior cornu down to and through the perichondrium.

From the Department of Otolaryngology, Presbyan Hospital, and the Department of Anatomy, Col- of Physicians & Surgeons, Columbia University.

1. Kelly, J. D.: Surgical Treatment of Bilateral alysis of the Abductor Muscles, Arch. Otolaryng. 293-304 (Feb.) 1941.

2. Orton, H. B.: Extralaryngeal Surgical Approach Arytenoidectomy: Bilateral Abductor Paralysis Larynx, Ann. Otol., Rhin. & Laryng. **53**:302-307 ne) 1944.

the posterior edge and on its mesial side sufficiently to free it of inferior constrictor attachments.

The facet-like joint between the inferior cornu and the cricoid cartilage is then separated, and the incision is carried through the perichondrium on the lateral wall of the cricoid cartilage and continued vertically upward until the cricoarytenoid joint is encountered (fig. 3). The joint is not separated until the subperichondrial dissection of the arytenoid cartilage has been accomplished. When the latter has been done, the joint is disarticulated, and all of the arytenoid is removed except that small anterior (nonarticular) free part closely associated with the vocal process.

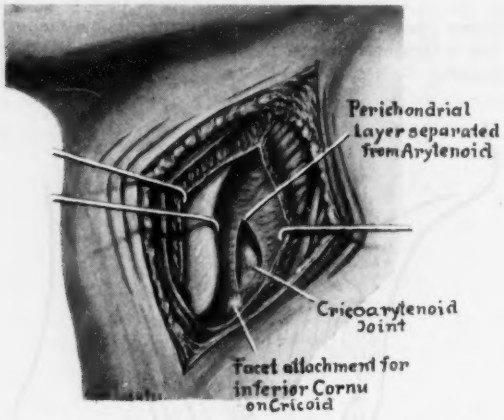


Fig. 3.—The perichondrium has been separated from the arytenoid.

A curved needle with chromic gut is passed around the vocal process, care being taken to keep it in the submucosa and to pass it through and include some of the fibers of the vocalis and the thyroarytenoideus muscles. The cord is then drawn laterally and sutured to the inferior cornu of the thyroid cartilage (fig. 4), and this in turn is reenforced by anchoring the suture to the anterior edge of the sternocleidomastoid muscle.

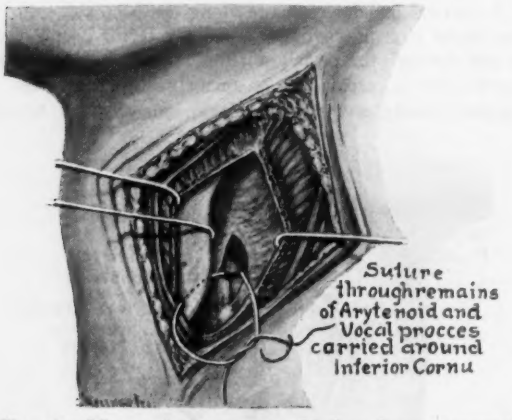


Fig. 4.—Most of the arytenoid has been removed. Chromic gut has been carried around the vocal process so that the cord may be drawn laterally and sutured to the inferior cornu of the thyroid cartilage.

Before the wound is closed, the larynx is inspected with the laryngoscope and careful note made of the position of the cord.

Closure is made by bringing the inferior constr muscle back into place with a few separate su Interrupted sutures close the skin, a Penrose being left in the lower end of the wound, whi removed in forty-eight hours.

REPORT OF A CASE

M. K., a man aged 45, was admitted to the June 19, 1944, complaining of occasional attack choking and difficulty in breathing. He stated he had been told that he had paralysis of both cords.

For the past twenty years he had had intermi attacks of choking. These attacks generally occ when he made an effort to clear his throat becau felt dry. His voice had been hoarse for years, an did not think that it had changed any.

In 1939 he underwent two operations on his thy gland for a toxic goiter. This reduced his nerv ness for a while but did not prevent his choking tacks. Six months prior to his admission to ward he had a recurrence of his thyrotoxicosis, w for three months prior to admission to our ward been under the care of the medical services. His b metabolic rate of plus 36 of three months before been reduced to minus 5. The medical services pressed the belief that he was sufficiently improved undergo an operation for the relief of his laryn paralysis.

The patient was a well developed and well nouris white man. Both eyes showed definite exophthalm The nares were clear but there was moderate de tion of the septum to the left. His sinuses transill nated well. The tonsils were small and chronic diseased. The ear drums appeared normal. The lar revealed bilateral abductor paralysis, with a very s airway. The heart and the lungs sounded nor The blood pressure was 110 systolic and 70 diastoli

The hemoglobin content of the blood was 100 cent; the red cell count, 5,230,000; the white count, 6,600, with polymorphonuclears 71, lymphoc 26, monocytes 1 and eosinophils 2. The Klein test negative. Urinalysis showed no glucose or albumi results of microscopic examination were normal. Ro gen studies of the chest and skull, a study of esophagus with barium sulfate and electrocardiogra examination all gave essentially negative results.

The patient was operated on, arytenoidectomy w lateral transposition of the right vocal cord being p formed on June 21. His tracheotomy tube was remo July 11. He was discharged from the hospital i proved July 17.

The patient has been followed up to the time of w ing (February 1945). He is now free of dyspnea all his regular activities, and he has had no furt choking attacks. His voice, while still hoarse, adequate for telephone conversation and carrying on business as a salesman.

COMMENT

This approach is made possible by the mobil of the thyroid cartilage, which is made e more mobile by the separation of the poster edge of the cartilage from the inferior constric muscle and by the separation of the infer cornu from its facet-like attachment to t cricoid cartilage.

his approach offers a relatively large field work in and adequate exposure, as one is ing and working directly down on the joint coarytenoid) instead of through a hole in the oid cartilage. Likewise it preserves the al thyroid cartilage, offering less trauma to patient, and leaves a firm structure on which nchor the transposed vocal cord.

SUMMARY

A posterior approach to external arytenoidectomy eliminates the necessity of making a window through the thyroid cartilage or removing the posterior half of the cartilage. The results in the cases in which the technic has been tried appear to justify this preliminary report.

156 East Thirty-Seventh Street.

SURGICAL TREATMENT OF CHRONIC FRONTAL SINUSITIS

SIMON JESBERG, M.D.
LOS ANGELES

Chronic disease of the paranasal sinuses offers its greatest challenge to therapy when the frontal sinus is the site of the infection. This cavity has problems peculiar to itself which make its successful surgical treatment more difficult than the treatment of any other nasal sinus.

The frontal sinus is the most poorly endowed by nature to withstand, or recover from, an infectious invasion. It is placed more deeply in dense bone, its lining membrane is thinner and more poorly nourished than that of the other sinuses and its drainage is the longest and the most devious. Being part and parcel of the ethmoid system and largely an outgrowth of those cells, its position, size and emptying mechanism are arranged to conform with the developmental vagaries of the ethmoid labyrinth. The nasal floor of the frontal sinus is mostly formed by the ethmoid bone, and therefore disease of the cells of the ethmoid bone often extends to the frontal sinus either directly or after blocking the frontal duct and impairing the drainage of the frontal sinus. It is obvious, then, that chronic infection of the frontal sinus almost always partakes of the same process in the contiguous cells of the ethmoid bone.

The indications and procedures for surgical treatment of the frontal sinus given by authorities, texts and treatises on the subject vary so much that when one is confronted by the necessity of treating a frontal sinus and seeks guidance, one finds such a morass of controversial ideas that one is utterly confused. One will find that the treatment of this sinus is probably less established in a uniform technic than that of any other. There are the conservatives, who apparently never use a surgical procedure unless there is an external fistula or unless the gravest symptoms are present, and the radicals, who are willing to operate on a sinus with minimal disease, which is represented perhaps only by indirect diagnostic findings, such as may be shown in a roentgenogram, and meager symptoms.

Read at the meeting of the Western Section of the American Laryngological, Rhinological and Otological Society in Los Angeles, Jan. 27, 1945.

Each surgeon must decide in his own m the indications for surgical intervention and course of procedure. In order to ascertain a careful study of the individual case from standpoints of anatomy and pathology is ne sary. When there is persistent discharge the frontal sinus, pain in or about this regio recurrent acute frontal sinusitis, the first sideration is that of putting the nasal pass in order. That is, any obstruction to the of the nose, whether septal, turbinal, ethmo or polypoid, should be corrected by an in nasal surgical procedure.

Invasion of the external tissue as represe by orbital phlegmon, abscess or fistula indic of course, that the bony walls of the sinus h been invaded by the infectious process.

Roentgenologic studies are indispensible determining the extent and the nature of involvement, as well as the anatomy of region.

One may well ask why infections of the fro sinuses are not treated in the same manner those of the mastoid process. That is, mod surgery demands complete ablation of the d eased tissue in the mastoid process, whereas the paranasal sinuses, particularly the frontal nuses, the many procedures that are propo seem content with partial removal of the disea tissue and amelioration of the patient's sy toms. Certainly those intranasal and other p cedures which do not completely remove diseased tissue or protect against reinfection not in accord with modern surgical princip

If the operations for obliterating the fro sinus proposed by Riedel [1] and Kuhnt [1] w followed, they would be analogous to the p cedures which are used in mastoidectomies, b the cosmetic deformity is rarely acceptable the surgeon or to his patient.

In order to achieve a satisfactory result the treatment of chronic frontal sinusitis, must remove all the diseased tissue and th either obliterate the entire cavity or provi

1. Cited by Loeb, H. W.: Operative Surgery of t Nose, Throat and Ear, St. Louis, C. V. Mosby Compa 1917, vol. 2, p. 70.

ble drainage for that part of the cavity that t obliterated.

e intranasal treatment of chronic frontal itis is a rather bad chapter in the history edicine because of its poor end results.

hile the procedure of removing obstructions e vault of the nose and establishing an ing in the frontal sinus through the anterior of the ethmoid labyrinth is occasionally essful, it can be so only if that opening ins freely patent and if, by the grace of God, iseased lining tissue undergoes some changes eby it is restored to a nonsuppurative state. happy outcome is not often observed.

e frontal sinus once having lost its empty- mechanism of ciliated epithelium and mucous must depend on gravity and air blasts to arge its contents into the nose. If this cial emptying mechanism cannot be main- d, sooner or later there is persistent or rent infection within the sinus.

tranasal operations on the frontal sinus can st be but uncertain. While they may pro- for a patent nasofrontal opening, they rarely it adequate removal of the diseased lining brane. Theoretically, the diseased lining brane might be removed from a small al sinus, but the operator could never be in of this with an intranasal operation. Pre- ably, he waits for the diseased lining mem- e to assume some semblance of health while inuing protracted treatment.

e external approach offers a plan for re- al of the diseased tissue in its entirety and is ttended by the many dangers of intranasal edures. The reluctance to accept external edures seems to be based on the fear of ng a cosmetic defect, but this need not tuate if the external operation is properly ned. In addition, the external procedures provide for the ablation of diseased tissues h could not be removed by the intranasal oach. In external approach the field is in plete view of the surgeon, and he can control removal of any tissue at will.

rophylactic treatment of chronic frontal sinu- begins with proper management of acute itis. An infection of the upper respiratory probably always is more or less associ- with sinusitis. If a restoration of health e nose can be brought about, the sinuses again restored to a condition of health. The rtance of spontaneous or assisted recov- from these acute infectious processes cannot verestimated, and intranasal treatment has reatest opportunity here. If there is failure estoration or recovery, there are brought about changes in the nasal and sinal mucosa that may lead to chronicity and a long train of pathologic events.

During these acute infections, intranasal instrumentation can but increase the danger of more extensive involvement of the sinuses. The simplest measures should be employed, such as shrinking with such agents as ephedrine or neosynephrine hydrochloride. Fracture of the middle turbinate, probing of the infundibulum and irrigation of the frontal sinus are sure to inflict additional traumas and are to be avoided. The exception to manipulation in acute infections of sinuses is early irrigative evacuation of the contents of an infected maxillary sinus.

In acute frontal sinusitis that is not responding to simple intranasal measures, an external trephining for drainage is most likely to result in restoration to normal. Intranasal surgical procedures for correction of obstructions or disease should be performed only after the acute symptoms have subsided. If these intranasal measures fail in restoring the frontal sinus to health, the surgeon must decide whether the prevalent symptoms justify further intranasal treatment, such as Proetz displacement, or whether he will resort to external opening of the frontal sinus. If he is convinced that the membrane of the frontal sinus is not returning to a healthy state, he should, beyond doubt, approach that sinus externally.

External approaches to frontal sinusotomy are numerous. The first to be offered definitely for treatment of this condition was recorded about 1750. Dr. Frank A. Burton showed the American Laryngological, Rhinological and Otological Society skulls which were removed from Aztec excavations in which some operation, presumably for relief of disease in this region, had been performed in a primitive manner.

Ogston,[2] in 1870, reported an operation which consisted of making an opening in the glabella and enlarging the frontal duct. Later, Ingals,[3] Good [4] and others proposed intranasal measures for draining the frontal sinus. Halle proposed an intranasal operation whereby a mucosal flap from the nose was utilized to keep the opening patent. Since that time many procedures have been proposed.

2. Ogston, cited by Loeb, H. W.: Operative Surgery of the Nose, Throat and Ear, St. Louis, C. V. Mosby Company, 1917, vol. 2, p. 62.

3. Ingals, cited by Loeb, H. W.: Operative Surgery of the Nose, Throat and Ear, St. Louis, C. V. Mosby Company, 1917, vol. 2, p. 69.

4. Good, cited by Loeb, H. W.: Operative Surgery of the Nose, Throat and Ear, St. Louis, C. V. Mosby Company, 1917, vol. 2, p. 66.

Probably the most important advance in surgery for the maintenance of a permanent opening was that described by Lothrop,[1] in which he removed the septum from within the frontal sinus, the bony tissue from within the sinus and the upper part of the nasal septum.

Sebileau,[5] in 1923, reported a similar procedure. Moulonguet and Demaldent [6] used a combination of the Lothrop and Sebileau operations with excellent results. They recommended using a unilateral incision opening the frontal sinus through the septum within the sinus and permitting the exudate to drain into the nose by way of a double passage.

It is quite certain that if the bone within the frontal sinus, including the nasal spine, and the upper part of the nasal septum are removed, there is provided an atrium between the nose and the frontal sinus that will remain permanently patent.

Fig. 1.—Supraorbital depression following ablation of a large frontal sinus. Note that there is no appreciable deformity unless the face is seen in profile.

The operation of Lothrop, which is performed through the glabella, cannot adequately remove diseased lining mucosa from the frontal sinus unless the sinus is small, nor can it adequately exenterate the contiguous tissues that are diseased in the ethmoid labyrinth.

The interposition of mucosal flaps from the nose or the transplantation of cutaneous grafts will, to a large measure, help to keep the naso-frontal opening patent, but a large frontal sinus that extends beyond the midline of the orbit will more than likely again become diseased as it cannot adequately empty itself even if such a permanent opening is provided.

5. Sebileau: Le plancher nas-frontal des sinus fronteaux, Zentralbl. f. Hals-, Nasen- u. Ohrenh., 1923, p. 341.

6. Moulonguet, A., and Demaldent, J. P.: Le traitement chirurgical des sinusitis frontales chroniques, Ann. d'oto-laryng., January 1936, p. 1.

In 1922 I first performed an operation wh by I employed the subbrow (Jansen-Ly incision and then removed all of the bone w the frontal sinus as well as the upper pa the nasal septum. I found that I had a view of the diseased ethmoid and frontal sin of the opposite side also and could sati torily treat them surgically. Since that I have been treating large frontal sinuses i same manner, with the addition of the re of all of the orbital and frontal wall of that of the frontal sinus that extends beyond the orbital line.

The deformity which is produced by th moval of the anterior and orbital walls o frontal sinus in its external part results in slight cosmetic defect or change in the pati appearance. Thus a large frontal sinus is verted into a small one which can contin a state of health, provided there is a patent i nasal opening.

The external part of the frontal sinus is collapsed by removing all of its bony including the orbital rim external to the mi of the orbit and thus permitting the soft ti to obliterate the outer part of the large fr sinus.

TECHNIC

These operations are preferably performed with patient under local anesthesia, preceded by basal cosis. Ninety minutes prior to the time of oper the patient is given by mouth 3 grains (0.19 Gm. pentobarbital sodium; thirty minutes later, ¼ g (0.016 Gm.) of morphine sulfate and 1/150 grain mg.) of scopolamine hydrobromide by hypodermic i tion. From then on he is given additional small dos appropriate amounts, of morphine sulfate by hypod injection and seconal sodium N. N. R. by mouth he is hard to arouse. Just prior to the time of oper the nose is sprayed with epinephrine hydrochl 1 : 5,000 and 2 per cent solution of cocaine hydrochl Cocaine crystals with epinephrine are applied w small applicator for intranasal nerve block to the re of the sphenopalatine, ethmoidal and anterior perfor nerves. After the external site of the operatio aseptically prepared and the patient is draped, the s injected with 1 per cent procaine hydrochloride epinephrine hydrochloride 1 : 50,000.

The points of injection are the tissues of the h head, the frontal nerve in the orbit, the ethmoidal n (intraorbital injection) and the infraorbital fora This has given, in my experience, such perfect anes that I rarely employ any other. It has a great ad tage over general anesthesia in that the field is al bloodless.

The Jansen-Lynch incision is made through the tissues and carried on down to the bone through periosteum. The trochlea and the lacrimal sac external to the periosteum and if this is stripped cl from the bone by sharp dissection, there will be n jury to these structures. If this procedure is ca out properly there will be no permanent ocular balance.

frontal sinus is opened in the oculofrontal angle the brow, and as much bone is removed as is sary to give a clear view and easy access to the There need be no restrictions in removing bony and as much as necessary of the os planum, the nal bone, the nasal bone or the frontal process of uperior maxilla can be sacrificed. In the ordinary teral frontal sinusotomy some consideration must iven to removing the external bony walls, for if

g. 2.—Jansen-Lynch incision; also an external brow ion for the lateral reaches of a large frontal sinus.

h of this external wall is removed the soft tissues d in and tend to obliterate the nasofrontal opening. the operation that I do this is of no importance, provide for a permanent nasofrontal opening by ving the bony tissues within the frontal sinus and emoving the upper part of the nasal septum.

rge frontal sinuses, particularly if there are supra- al cells of the ethmoid labyrinth, must be completely obliterated. The little angles where the external plate and the inner plate join, whether ethmoidal or frontal, must have their lining membrane completely removed, and the outer table must be so removed that there will be no overhang. In large frontal sinuses an additional incision is made straight throught the brow from the midorbital line as far laterally as necessary. The periosteum is reflected upward and downward exposing the external supraorbital region as well as the outer half of the bony orbit. One tries to preserve the frontal nerve and its supraorbital branch if possible. Should there be a break in the ethmoidal or in the sphenopalatine arteries, the field is wide open, and the bleeding is readily controlled by electrocoagulation.

Now these external incisions are completely closed. A petrolatum gauze trailer is placed in the frontal cavity and brought out into the nose for protection against hemorrhage.

If the infectious process is suspected of being virulent or if the dura or the cortex has been uncovered, a small rubber tube may be left in the external wound for instillation of a solution of a penicillin salt.

These procedures provide for establishing between the nose and the frontal sinuses a permanent atrium, one which cannot close. They give complete access to diseased areas and permit thorough eradication of the pathologic tissue. Large frontal sinuses are thus converted into small cavities which can better drain into the nose and remain in a state of health.

The cosmetic results are excellent and do not change the physiognomy of the patient. Even with a large temporal defect, which can be observed only by close inspection, the patient is not embarrassed by change in appearance, and his close associates fail to appreciate his altered anatomy.

500 South Lucas Avenue.

Case Reports

BACTERIAL THROMBOPHLEBITIS OF A CAVERNOUS SINUS WITH RECOVE

ROBERT F. WELTY, M.D., PHILADELPHIA

Infections about the region of the face have long been treated with great respect and special care because of the constant threat of involvement of the cavernous sinus and the almost invariably fatal outcome of this complication.

As late as 1936, Grove,[1] in reviewing this subject, reported a mortality of almost 100 per cent. As to the occasional reports of recovery, the accuracy of the diagnosis in many has been questioned, orbital cellulitis, especially, being at times a problematic possibility in differential diagnosis.

In his monograph on thrombophlebitis of the cavernous sinus, Eagleton [2] listed certain criteria for establishing the diagnosis, namely:

1. A known site of infection.
2. An infection of the blood stream.
3. Early signs of venous obstruction.
4. Involvement of nerves in the sinus.
5. A neighborhood abscess of the soft parts.
6. Symptoms of complicating disease.

The concept of cavernous sinus thrombosis as contrasted with cavernous sinus thrombophlebitis has been stressed by many authors.[3] In both conditions striking signs are noted locally on examination. In the former, however, the infection remains outside the lumen of the sinus and induces thrombosis of a sterile type. In the latter, the clot is a septic one, and there is the associated clinical picture of septicemia. Most of the recoveries reported fall into the class of aseptic thrombosis. Le Marquand and Recordon [4] have recently recorded a case of aseptic cavernous sinus thrombosis with rapid and complete recovery, in which there was advanced bilateral involvement with no element of infection evident, the temperature never rising ab 99.4 F. throughout the illness.

Prior to the introduction of chemother many attempts were made to treat disease of cavernous sinus by operation. The results, h ever, were in general unsatisfactory, and m authors reached the conclusion that the surv rate was just as great with conservative treatm as with operative intervention.[5]

With the advent of sulfonamide compou as therapeutic agents, occasional reports be to appear of recoveries following undoub bacteremic thrombophlebitis of the caver sinus.[6]

In well over 50 per cent of cases of disease the cavernous sinus the thrombosis extends involve the opposite side. A further advanc the treatment of this disease was made Lyons [7a] and Schall [7b,c] with the introduction heparin therapy to limit further extension of

From the surgical service of Dr. Eldridge L. Eliason at the Hospital of the University of Pennsylvania.

Read before the meeting of the section on otolaryngology of the College of Physicians and the Philadelphia Laryngological Society, in Philadelphia, Dec. 20, 1944.

1. Grove, W. E.: Septic and Aseptic Types of Thrombosis of the Cavernous Sinus, Arch. Otolaryng. **24**:29-51 (July) 1936.

2. Eagleton, W. P.: Cavernous Sinus Thrombophlebitis, New York, The Macmillan Company, 1926.

3. (*a*) Cavenaugh, J. B.: Cavernous Sinus Thrombosis: A Study of the Cases of Recovery, Brit. M. J. **1**: 1195-1199 (June 13) 1936. (*b*) Kopetzky, S. J.: Thrombosis of the Cavernous Sinus, with Bilateral Blindness Cured by an Unorthodox Procedure, Ann. Otol., Rhin. & Laryng. **50**:284-286 (March) 1941. (*c*) Grove.[1]

4. Le Marquand, H. S., and Recordon, E. G.: Aseptic Cavernous Sinus Thrombosis with Recovery, Lancet **1**:247-248 (Feb. 19) 1944.

5. Grove.[1] Kopetzky.[3b]

6. (*a*) MacNeal, W. J., and Cavallo, M. E.: St tococcic Bacteremia and Apparent Thrombosis of Cavernous Sinus with Recovery, J. A. M. A. **109**:2 2141 (Dec. 25) 1937. (*b*) Barnshaw, H. D.: Report Case of Bilateral Cavernous Sinus Thrombosis: covery Without Operative Intervention, J. M. Soc. N Jersey **36**:22-24 (Jan.) 1939. (*c*) Seydell, E. Recovery from Thrombosis of the Cavernous Si Arch. Otolaryng. **30**:429-430 (Sept.) 1939. (*d*) M rison, L. F., and Schindler, M.: Cavernous Si Thrombosis: Report of Recovery Following Sulfa dine Therapy, ibid. **31**:948-954 (June) 1940. (*e*) W C. T., and Wolfe, W. C.: Thrombosis of the Caver Sinus with Recovery, ibid. **33**:81-85 (Jan.) 1941. Shemp, H. I.; Afremow, M. L., and Rhoads, P. Thrombosis of the Cavernous Sinus with Staphyloco Septicemia Treated by Intravenous Injection of So Sulfathiazole with Recovery, ibid. **34**:1025-1028 (N 1941. (*g*) Eichhorn, J. P.: Cavernous Sinus Thrombo Recovery Following Treatment with Sulfathiazole, O State M. J. **37**:1076-1077 (Nov.) 1941. (*h*) Moore, B.; Gardner, J. D.; Bell, K. R., and Tannenbaum, A. Cavernous Sinus Thrombophlebitis: Cure with Su thiazole, J. A. M. A. **119**:708-710 (June 27) 1942. Bradlow, B. A.: Recovery After Cavernous Si Thrombosis, South African M. J. **16**:287-288 (Aug. 1942. (*j*) Doorly, A. R. C.: Thrombophlebitis of Cavernous Sinus: Recovery, Brit. M. J. **1**:42 (Jan. 1943. (*k*) Doyle, P. H.: A Case of Cavernous Si Thrombosis with Recovery, M. J. Australia **1**:363 (A 24) 1943. (*l*) Aufses, A. H.: Cavernous Sinus Thro bosis with Recovery: Case Report, J. Mt. Sinai H **10**:471-474 (Nov.-Dec.) 1943. (*m*) Fuller, H.: Ca nous Sinus Thrombosis with Recovery: Report Case, J. Florida M. A. **30**:238-240 (Dec.) 1943. Trevor-Roper, P. D.: A Case of Cavernous Si Thrombosis, Brit. M. J. **1**:255 (Feb. 19) 1944.

(Footnotes continued on next page)

mbus. Since penicillin has proved to be an tive chemotherapeutic agent, one might ex- that another potent weapon is available for treatment of disease of the cavernous sinus. he following pages I report a case of staphylo- ic thrombophlebitis of the cavernous sinus which treatment with sulfadiazine, penicillin heparin brought about recovery. Schall [7b] Lyons [7a] administered heparin by continuous venous drip at such a rate as to maintain tting time of ninety minutes. Since heparin introduced into the therapy of this dis- some have hesitated to use the drug be- e of the extensive bleeding, especially into brain, which at times has followed its use.[6h] associates and I decided, however, that a erate situation justified the possible risk. eemed to us that prolongation of the clotting to ninety minutes might be unnecessary, we were satisfied to attempt to keep the ing time at twenty to thirty minutes, thereby ucing the risk from hemorrhage.

REPORT OF A CASE

n Sept. 20, 1944, a 13 year old white boy was itted to Dr. Eliason's service at the Hospital of the

Fig. 1.—Photograph at the time of admission.

versity of Pennsylvania because of a spreading ction involving the right cheek and orbital region. our days before, a furuncle had developed on the r aspect of the right ala nasi. The infection appar- y remained rather well limited for three days, with local symptoms of pain, tenderness and swelling. the day preceding admission the mother had noted no nificant swelling of the cheek or the eyelids. The following morning, however, the boy wakened with pronounced redness and swelling extending over the right cheek and about the eye, leading to almost complete closure of the lids. He was taken to the family doctor, who immediately referred him to the hospital.

On examination he was found to be alert and oriented and could furnish his own history. However, his temperature was 104.8 F., and obviously he was critically ill.

There were marked edema, redness and tenderness about the right eye and over the frontal and malar regions on that side. The lids were swollen shut. The globe was proptosed and immobile. Chemosis was

Fig. 2.—Photograph at the time of discharge.

marked. No view of the fundus could be obtained. The left eye showed no involvement of the lids, the extraocular muscles or the fundus.

The right nostril was obstructed by a bloody purulent discharge from the furuncle. The anterior cervical nodes were enlarged and tender. There was no nuchal rigidity, and Kernig's sign was not present.

The total white blood cell count was 19,600. Blood culture on admission showed 65 colonies of hemolytic Staphylococcus aureus per cubic centimeter.

A diganosis of thrombophlebitis of the cavernous sinus was made, and the patient was given 200,000 units of penicillin intramuscularly every twenty-four hours. In addition, sodium sulfadiazine was given intravenously in a dosage of 1.0 Gm. every six hours. The administration of heparin also was started the day of admission. The initial dose was 3.3 cc. intravenously. This was followed by 4.0 cc. (4,400 units) intramuscularly every six hours.

Later during the day of admission he began to vomit, and intravenous injection of fluids was started to maintain his intake of fluids. He became increasingly confused and finally stuporous.

The following day the edema had extended to involve the left frontal region. The lids of the left eye were also markedly swollen, though the globe was not proptosed and movements of the extraocular muscles were full.

In addition, at that time, nuchal rigidity developed, and Kernig's sign was present. Lumbar puncture revealed a pressure of 260 mm. of water. The fluid was turbid.

7. (*a*) Lyons, C.: The Treatment of Staphylococcal ernous Sinus Thrombophlebitis with Heparin and motherapy, Ann. Surg. **113**:113-117 (Jan.) 1941. (*b*) all, L. A.: Treatment of Septic Thrombophlebitis of Cavernous Sinus, J. A. M. A. **117**:581-584 (Aug. 23) ; (*c*) Cavernous Sinus Thrombophlebitis, Mississi Doctor **19**:398-401 (May) 1942.

Immediately 10,000 units of penicillin was injected intraspinally. Examination of a specimen of the spinal fluid at this time revealed 1,120 white blood cells per cubic millimeter, the majority of which were polymorphonuclear leukocytes. The protein value was 82 mg. per hundred cubic centimeters. Both smear and culture of the spinal fluid failed to demonstrate any organisms.

Because of his increasingly serious condition, the administration of penicillin was changed from the intramuscular to the intravenous route. This was supplemented by an intracisternal injection of 20,000 to 40,000 units of penicillin every twelve hours for six days.

From the first the ophthalmologists had considered the possibility of orbital cellulitis with abscess formation. On the fourth day, with the patient under ether anesthesia, the orbit was explored both above and below the globe, with negative results. A blood culture made on the same day was negative. Edema over the right mastoid region was noted at this time—a finding considered by some to be positive evidence of an involvement of the cavernous sinus in contrast to simple orbital cellulitis.

By the seventh day he had become quite rational and from then on showed continued clinical improvement. The findings became localized entirely to the region about the right eye. The return of extraocular movements was rapid and complete except for persistent sixth nerve paralysis and some ptosis of the upper lid. Corneal sensation, which had initially been impaired, returned to normal.

On the tenth day the intravenous medication was continued. Sulfadiazine was given by mouth and penicillin intramuscularly. On the twelfth day the sulfadiazine therapy was discontinued, and the dosage of penicillin was reduced. Four days later the heparin therapy was discontinued, but the administration of penicillin was maintained until the twenty-third day. The patient was discharged from the hospital four days later.

In summary, the treatment consisted of:

(*a*) 46 Gm. of sulfadiazine, administered over a period of twelve days; (*b*) 280,000 units of heparin, injected over a period of sixteen days; (*c*) 3,600,000 units of penicillin, given over a period of twenty-three days, the majority of the doses being given intravenously during the first ten days.

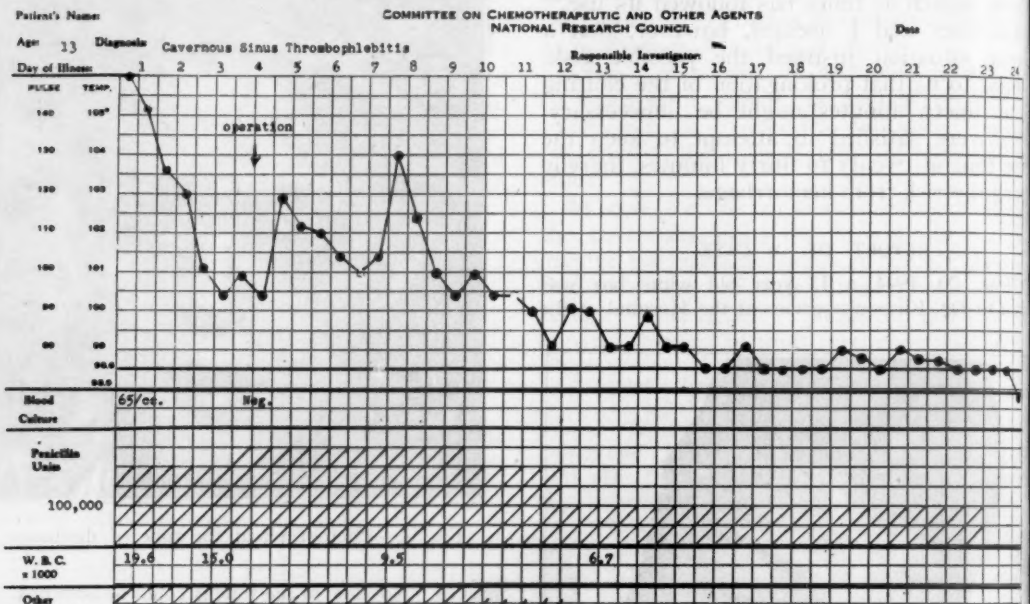


Fig. 3.—Graph of temperature and medications.

He has been seen several times since discharge. Vision is 6/6 in the left eye and 6/12 in the right eye. There is still some weakness of the external rectus muscle and slight ptosis of the lid. These are sequelae which have been noted by others,[8] and further return of function is anticipated.

ACKNOWLEDGMENT

Dr. Karl Houser, Dr. Francis Grant and Dr. Frank Adler and their staffs in the departments of otolaryngology, neurosurgery and ophthalmology gave advice and assistance in the care of the patient.

8. Doyle.[6k] Aufses.[6l] Fuller.[6m]

Progress in Otolaryngology

Summaries of the Bibliographic Material Available in the Field of Otolaryngology

ALLERGY

ERNEST L. MacQUIDDY, M.D.
AND
R. E. KING, PH.D.
OMAHA

The Army Medical Corps continues to recog- the importance of allergy since it causes a of considerable time in training and sub- ent combat. Statistics from the Army Air ces Regional Hospital of the San Antonio, as, Aviation Cadet Center are presented by pton and Rand.[1] From Aug. 1, 1942 to 1, 1943, 1,541 new cases were examined in llergy section of this hospital. Of the men ving the certificate of disablity for discharge, per cent had allergic diseases. Nine hundred twenty-one of the 1,238 men with allergic ses had respiratory allergy, hay fever, vaso- r rhinitis and bronchial asthma; 7.48 per had bronchial asthma. The greatest prob- was intrinsic bronchial asthma associated chronic respiratory infection.

similar experience is reported from the gy section of the Station Hospital, Camp ding, Fla. Gold and Bazemore[2] state that er cent of the patients were admitted for ma, while 11 per cent were admitted for fever, 3.59 per cent for allergic rhinitis and r cent for migraine. Of all those examined use of asthma, 24 per cent were discharged the service, 14 per cent were returned to duty and 19.6 per cent were reclassified to ed duty. Most of these received desensiti- n treatment. Fifty-eight per cent of their matic patients were successfully rehabili- as soldiers. Of the men discharged, 65 cent had less than six months' service and per cent had less than thirty days' service to discharge. In order to cut down the ber of men receiving an early medical dis- ge, it was decided that all patients with a ry of allergy should have special studies of allergy prior to induction. The local induc- station referred inductees to the allergy section of the Station Hospital, where they were hospitalized for a period of three days. During this time they received routine studies, which were based on a complete history, a physical examination, a Kahn test, a complete blood count, a urinalysis, a study of the sputum, nasal smears for eosinophils, electrocardiograms, roentgenograms of the chest and cutaneous tests. These tests were not regarded as conclusive in the effort to arrive at a final recommendation but were evaluated together with the patient's civilian occupation and ability to stand certain types of work. Bronchial asthma was diagnosed in 132 of the 143 inductees so studied. Forty-two per cent were recommended for rejection. These men would have received disability discharges in less than six months had they been accepted.

Shahon[3] discusses some of the difficulties the examining physician meets in the effort to rule out allergic persons at induction centers. He lists important questions for the detection of allergic manifestations in prospective soldiers and discusses some of the benefits to which the honorably dsicharged soldier is entitled.

French and Halpin[4] discuss the military management of allergic disease in the Fourth Service Command. Eighty-nine allergy clinics have been established, which all function as a unit by having a central laboratory prepare the standardized allergenic extracts. By receiving a prompt diagnosis and thorough specific therapy, the allergic soldier is able to remain on a full duty status. Allergy wards have been established in those hospitals of sufficient size to warrant such a procedure. This insures better care and more rapid disposition of the hospitalized allergic patient.

The greatest single cause for hospitalization has been bronchial asthma. Of 1,153 patients

1. Hampton, S. F., and Rand, H.: The Problem of gy at an Army Air Forces Hospital: I. Respiratory lergy (Hay Fever, Vasomotor Rhinitis and Bronchial thma), J. Allergy **15**:355-368, 1944.

2. Gold, E. M., and Bazemore, J. M.: Significance of lergy in Military Medicine, J. Allergy **15**:279-282, 1944.

3. Shahon, H. I.: Allergic Problem of the Inductee, the Soldier and the Veteran, Ann. Allergy **2**:413-423, 1944.

4. French, S. A., and Halpin, L. J.: Military Management of Allergic Disease, J. Iowa M. Soc. **34**:272-274, 1944.

in the allergy wards over a period of six months, 820 had bronchial asthma. Six hundred and thirty-six of these patients were returned to duty as a result of allergic investigation and therapy, and only 194 were given a certificate of disability discharge. Military management cannot possibly yield results comparable to those obtained in civilian practice, because environment cannot always be controlled. Feather-free and dust-free sleeping quarters cannot be obtained in a barracks housing 30 to 40 men. Restricted diet in the average army mess is an impossibility. In spite of these difficulties, beneficial results are obtained in proper military management of the allergic diseases. Of the allergic patients appearing before disposition boards over a period of six months, almost twice as many were retained in the service under treatment and without disabling symptoms as were discharged from the army.

French and Halpin [5] present interesting statistics compiled from 67 of the 89 allergy clinics of the Fourth Service Command for 1943. A total of 32,046 patients were seen. This included 6,842 with dermatitis caused by poison ivy, diagnosed in 50 clinics. Of the 25,204 patients with allergic symptoms of primary importance, 23,419 were of military status and 1,785 were civilian dependents. Of the total number of patients, 5,373 were given specific pollen therapy for seasonal hay fever; ragweed pollen was the greatest offender. There were 946 patients with seasonal bronchial asthma, while 1,384 had symptoms of both seasonal hay fever and bronchial asthma. Perennial bronchial asthma was responsible for the appearance of 7,261 patients at the 67 allergy clinics. Most of these were proved sensitive to dust by history and by cutaneous test. Other etiologic factors were chiefly of the inhalant type. Persistent year-round complaints of nasal congestion and discharge brought 3,831 patients to the allergy clinics. The allergic rhinitis was not particularly disabling, but the persistent symptoms caused much discomfort. Other manifestations of allergy were urticaria in 1,644 patients, migraine in 819, gastrointestinal disturbance in 255 and food antipathies in 1,565. The report also shows that over a period of twelve months 8,139 allergic patients were admitted to the hospital wards and that in only 602 of these was uncomplicated seasonal hay fever of sufficient severity to warrant absence from duty diagnosed. These patients spent 172,455 days in hospitals, an average of 21.2 days for each patient. Of the allergic patients, 3,742 were discharged, while 10,573 were reclas and returned to a type of duty consistent their complaints.

Alford [6] studied the first 100 patients bronchial asthma admitted to Percy Jones eral Hospital and has recorded certain info tion of interest and value. These patients re sented about 10 per cent of the medical ad sions at the time. They were tested with m and mold extracts secured by culture of ma from moldy leather goods brought back by tients from the South Pacific. Extracts were made from the dust secured from their barr bags. Attacks of asthma were induced when inhaled the dust of these barracks bags, a patient had a severe attack of asthma after re ing an injection of 0.1 cc. of a concentr extract of overseas dust. This overseas usually produced a larger wheal than the U. S. A. dust. Nitrogen determinations sho the overseas dust to contain twenty time much nitrogen as the stock U. S. A. The tests with mold extracts were not clusive. The asthma of those in service in South Pacific was thought to be caused b combination of dust, molds and dampness. was concluded that in the disposition of t allergic patients, soldiers with asthma, migr or dermatologic allergies should be discha unless the medical officer could find a g reason for keeping them in the service. It further stated that soldiers with bronc asthma might be placed on nonstrenuous du (*a*) "attacks are due to a single sensitivity which rapid, adequate treatment is avail (*b*) attacks are mild or infrequent, not p venting light duties, (*c*) the initial attack overseas, and (*d*) the attack in the army w recurrence from childhood."

Todd [7] also states that major allergy, e present at the time of induction or show occur by the personal and the family history in doubtful cases, by tests with key allerg should be a denying factor for admission the combat forces. However, a compens symptom-free subject of allergy can be used limited service. The subject of asthma is left out of consideration by selective service, before changes were made in the physical requ ments, many thousands were taken in who now hampering the medical departments will be able to establish connection for disab compensation.

5. French, S. A., and Halpin, L. J.: Army Allergy: Fourth Service Command 1943, Ann. Allergy **2**:365-379, 1944.

6. Alford, R. I.: Disposition of Soldiers with B chial Asthma, J. Allergy **15**:196-202, 1944.

7. Todd, L. C.: Some Military Considerations o Allergic Individual, South. Med. & Surg. **106**:2 1944.

comparative report concerning the work on the ear, nose and throat in the army at and overseas has been published by ll.[8] He reports on the first thousand cases hich he administered treatment during his e as an "army E.N.T. specialist" in a mili- hospital in England and also in a general tal, working with the British North African . There was an overseas increase in otitis na, acute otitis media and atrophic rhinitis, decrease in allergy in the North African tal. These differences were thought to be o climatic variations.

RGY AFFECTING EAR, NOSE AND THROAT

e otolaryngologist should be allergy minded. [9] in discussing this problem stated that r cent of new patients coming to his clinic se of nasal symptoms for a six month period January to July were found to be allergic. urther stated that in the majority of such nts an allergic study will disclose the cause e symptoms, and proper treatment bring relief without resort to nasal treatment or cal intervention.

nes[10] states that the otolaryngologist should dequately trained in the diagnosis and the ment of allergic nasal conditions. Even in clinics where the otolaryngologist and the gist may work together, he must have suf- nt knowledge of allergic conditions to make iagnosis and to manage the case. He recom- ls that otolaryngologists equip themselves extracts for making scratch and endermic . These extracts should include pollens, s, dust, bacterial preparations and miscel- ous groups. In addition, the symptomatic ment must not be forgotten. Many allergic nts react favorably to histaminase, and some benefited by "the administration of diluted ochloric acid U.S.P., 5 to 20 minim doses in an adequate quantity of water after each ."

discussing the relation of infection to aller- conditions in the nose, Ellis[11] states that nts with vasomotor rhinitis and other aller- nasal manifestations should have enough ical treatment to give good drainage, as the ence of infection may intensify the allergic symptoms. When the infection is eliminated, the symptoms of allergy may not be noticeable. Therapy for allergy must be instituted, however, if symptoms of allergy are still present after adequate drainage.

Williams[12] reports what he terms the "syndrome of intrinsic allergy." This is an interrelated group of painful symptoms about the head and can be broken down into four main divisions, namely, into vasomotor rhinitis, Ménière's syndrome, myalgia and the vasodilating pain syndrome. These main divisions may occur singly, but often careful investigation will show many signs and symptoms of the other main divisions to be present also. These are all interrelated components of a syndrome of physical allergy.

Craft[13] in describing some unusual manifestations of nasal allergy discusses a case in which there was severe pain in the upper teeth and antral regions of both sides, accompanied by moderate nasal blocking. The patient was found to be sensitive to house dust. Desensitization with house dust completely relieved the neuralgia and the nasal symptoms.

In discussing physical allergy as an etiologic factor in paranasal sinus disease, Andes[14] states that chilling drafts about the face and the neck present one of the most important problems of all. The actual effect which the cold draft produces is not known. Reflex vasodilatation of the nasal tissues and momentary leukopenia are only a part of the total picture. The worst effect follows sleeping in a cold room with the windows open. Undoubtedly this American fad causes a needless amount of sinus disease and suffering. Drafts about the head and the neck especially should be avoided. Other important physical factors of allergy discussed are cold, humidity of the air, dust, swimming and diving and meteorologic causes. Certain patients with sinus disease can closely connect their attacks with atmospheric changes. It seems that certain persons merely have nasal tissues that are unusually sensitive to such atmospheric disturbances.

In discussing the symptoms and the methods employed in the diagnosis of sinusitis, Thornell[15] states that anosmia may be present and is not definitely related to the sinusitis. It may be due to generalized nasal congestion, polypoid

Birrell, J. F.: A Comparative Report on Ear, and Throat Work in the Army at Home and Over- J. Laryng. & Otol. **59**:16-31, 1944.

King, E.: Why Otolaryngologists Should Be rgy-Minded, Ohio State M. J. **40**:138-140, 1944.

Jones, E. H.: Allergic Problems in Otolaryn- gy, Mississippi Doctor **21**:220-224, 1944.

Ellis, B. E.: Relation of Infection to Allergic es in the Nose, Tr. Indiana Acad. Ophth. & Oto- ng. **28**:30-37, 1944.

12. Williams, H. L.: Intrinsic Allergy as It Affects the Eye, Nose and Throat: The Intrinsic Allergy Syndrome, Ann. Otol., Rhin. & Laryng. **53**:397-443, 1944.

13. Craft, K. L.: Some Unusual Manifestations of Nasal Allergy, J. Indiana M. A. **37**:180-184, 1944.

14. Andes, J. E.: Physical Allergy and Paranasal Sinus Disease, Journal-Lancet **64**:384-388, 1944.

15. Thornell, W. C.: Symptoms and Methods Employed in Diagnosis of Sinusitis, Proc. Staff Meet., Mayo Clin. **19**:470-472, 1944.

developments or degenerative changes in the olfactory region. Nasal polyps when present may or may not be due to allergy. Inspection of the nasal passages and posterior rhinoscopy with the aid of a nasopharyngeal mirror or a nasopharyngoscope are helpful in locating the involved sinuses. Transillumination is of significance only when it reveals no abnormality; it is not used routinely as a diagnostic procedure because of anatomic variations of the sinuses which may be present. The roentgenogram is an important and essential laboratory aid in diagnosing sinusitis. Its greatest use is to reveal the anatomic arrangement of the sinuses.

Hallberg [16] states that roentgenologic examination should be made in all cases in which pus, changes in the mucous membrane, allergic conditions, polyps or other signs of disease are observed in the nose in the course of routine examinations of the ears, the nose and the throat.

In discussing the pathologic changes in sinusitis, Brown [17] stated that the finding of characteristic chronic hyperplastic sinusitis is polypoid hyperplasia of the mucous membrane. No pus is found in the sinus. The mucous membrane of the patient with the allergic type of sinusitis is similar to that of the patient with the hyperplastic type except that it is paler and more edematous and contains numerous esoinophils. Pus is not found here but may be found in the mixed type of chronic sinusitis.

Hyperplastic sinusitis, which Williams [18] defines as a mixture of allergic and infectious sinusitis, is commonly accompanied by a bizarre reference of pain, in a distribution inexplicable on the basis of the known distribution of the sensory nerves. These patients present themselves to the physician with the self diagnosis of sinus headache, and it is the allergy rather than the infection which is responsible for the symptoms. It is paramount to recognize the allergic background and give treatment for that along with the necessary surgical procedures if relief is to be secured.

Richards [19] discusses four decades of nasal allergy. He stresses the importance of a complete history, a careful nasal examination, a painstaking and repeated cytologic study of the nasal secretions, an appreciation of the role of other manifestations of allergy and a therapeutic approach based on all these to give the pr day rhinologist a better working backgr than he has heretofore enjoyed. Special is laid on the fallacy of the opinion that all discharge is indicative of infection and o importance of differentiating between recu common cold and nasal allergy. As a r unnecessary and inappropriate nasal opera are being performed less and less. There specific therapeutic solution to the proble nasal allergy. During the past four de numerous hopeful approaches have led to alleys. Invaluable help has been afforded b allergists and the immunologists, who shown that the rhinologic aspect of aller only one of its manifestations. The solut the problem today lies in the collaboration various groups of workers in special fields.

EYE

Allergic kerotoconjunctivitis is rare. Linh gives an analysis of 54 cases of conjunct and keratitis of allergic origin. Thirty- of the patients had either acute or chronic junctivitis, and 17 had keratitis. Twenty- of the patients gave histories of allergy i immediate family, and 20 had previous sea symptoms. Twenty-five presented sympto itching of the eyes or lids, 18 complained c of watering of one or both eyes and 18 o ness of the eyeballs. Nine had as their complaint sore, itchy, swollen or irritated Blurred vision was a symptom of only 4 pat Laboratory tests revealed a negative Kahn tion, and eosinophils were present in the b of only 35 of the patients. The average was 2.9 per cent. Differential counts for e ophils were made on smears of material the conjunctivas of 19 patients. The av count was 4 per cent. The values varied 0 to 12 per cent. In general, the eosin count seemed to be much higher when the reaction was more acute, but no definite re could be found between the eosinophil co the blood and that of the smear. Forty- patients had cutaneous tests with 90 aller including bacteria. Acute reactions were tained for the following allergens in 1 pa each: sycamore, horse serum, corn meal, to monilin, buckwheat, feathers, wool and ra Two patients showed 4 plus reactions to tr phytin. In only 2 patients who gave 4 reactions was the allergen one of the ten common allergens. These patients were tr by desensitization. Seven showed an a

16. Hallberg, O. E.: Roentgenologic Aspects of the Paranasal Sinuses, Proc. Staff Meet., Mayo Clin. **19**: 472-473, 1944.

17. Brown, H. A.: Pathologic Changes in Sinusitis, Proc. Staff Meet., Mayo Clin. **19**:468-470, 1944.

18. Williams, H. L.: The Treatment of Sinusitis, Proc. Staff Meet., Mayo Clin. **19**:474-479, 1944.

19. Richards, L.: Four Decades of Nasal Allergy, Arch. Otolaryng. **39**:465-469 (June) 1944.

20. Linhart, W. O.: Conjunctivitis and Kerati Allergic Origin: Analysis of Fifty-Four Cases, Ophth. **31**:403-407 (May) 1944.

erbation of the disease at some time early
e desensitization treatment, at which time
lose was decreased but treatment was con-
d. For all patients the prognosis was good,
it was believed that allergic desensitization
uced improvement in all but 6 who were
tive to such a great number of substances
could not be desensitized.

ccording to Koch,[21] any or all of the ocular
es may manifest allergic activity. External
rbances are much more common than those
rring internally. Cutaneous allergy of the
is similar to cutaneous allergy in general.
ay be associated with conjunctival reaction
be responsible for it. Phlyctenular kerato-
unctivitis is regarded as an allergic mani-
tion to tuberculoprotein. Allergic episcle-
and scleritis are probably initiated by circu-
g allergens and are therefore a difficult
nostic problem. Allergic manifestations in
uveal tract range from mild iritis accom-
ing infections of the upper respiratory tract
hose seen in sympathetic ophthalmia. In
y persons with atopic dermatitis lens opaci-
eventually develop; the lens being of ecto-
nal origin may be an important factor.

iboflavanosis has been discussed as a prob-
cause of vernal conjunctivitis by A. L. Castel-
s.[22] He bases his opinion on observation of
patients, 92 per cent of whom showed im-
iate improvement in their condition follow-
treatment with riboflavin. It is believed that
eficiency of riboflavin interferes with the
hanisms of oxidation in the tissues and that
lesions of the skin and the mucosa may be
to local disturbances of cellular nutrition
respiration. The ocular changes may result
local cellular anoxia. These patients were
ed with 1 to 3 (1 mg.) tablets of riboflavin.
ptomatic therapy consisted of a few drops
tetracaine hydrochloride and epinephrine
ochloride in distilled water, the solution to
sed only when symptoms were accentuated.
ty-five of the patients showed improvement
ll ocular symptoms on the third or fourth
Sixty-two showed improvement in ten to
en days, and the rest, 9 patients, did not
rn for examination. It is necessary, how-
, to continue administration of the riboflavin
ast during the summer, when the symptoms
ar. The following year it is advisable to start the treatment before the warm weather begins, to prevent recurrence of the symptoms.

Lehrfeld,[23] however, does not agree that ariboflavinosis is a probable cause of vernal conjunctivitis. He states that vernal conjunctivitis is purely an ocular manifestation of an allergic state. He cites the periodicity of vernal conjunctivitis, appearing during the summer in correspondence with the pollenation of trees, grasses and weeds; the observation that it is intensified by heat and humidity and that the symptoms are promptly relieved by the use of epinephrine or epinephrine-like products is characteristic of allergic manifestations. Furthermore, the clinical symptoms of vernal conjunctivitis have been produced out of season by inserting pollens to which the patient is sensitive into the conjunctival cul-de-sac.

In a comparison of the eyes of pigmented and albino rabbits reacting to normal horse serum given by intraocular followed by intravenous injection, Schlaegel[24] found that the gross and microscopic ocular reactions were essentially the same in pigmented and albino rabbits. The reactions were most pronounced when the intravenous followed the intraocular injection by fourteen days but were not as great as when sensitization was carried out intradermally prior to intraocular injection. The microscopic picture of the injected eyes showing severe reactions bore a close resemblance to that of sympathetic ophthalmia.

It has also been determined by Scobee and Slaughter,[25] experimenting on rabbit eyes, that cutaneous sensitivity to lens substance can be induced by repeated and coincident injections of staphylococcus toxin plus lens substance. When the eyes of such sensitive rabbits are needled, a clinical and histologic picture develops that resembles enophthalmitis phacoanaphylactica in man.

HISTAMINE

Code[26] gives an interesting discusssion on the role of histamine in the production of anaphylactic and allergic reactions. Histamine is normally present in the white cell elements of the blood of most species of animals. During severe

Koch, F. L.: Ophthalmologic Expression of
gy, Eye, Ear, Nose & Throat Monthly **23**:483-487

Castellanos, A. L.: Ariboflavinosis as a Probable
e of Vernal Conjunctivitis, Arch. Ophth. **31**:214-
(March) 1944.

23. Lehrfeld, L.: Vernal Conjunctivitis, Correspondence, Arch. Ophth. **31**:557-558 (June) 1944.

24. Schlaegel, T. F., Jr.: Comparison of Ocular Reactions of Pigmented and Albino Rabbits to Normal Horse Serum: Intraocular Followed by Intravenous Injection, Am. J. Ophth. **27**:137-146, 1944.

25. Scobee, R. G., and Slaughter, H. C.: Enophthalmitis Phacoanaphylactica, Am. J. Ophth. **27**:49-52, 1944.

26. Code, C. F.: Mechanism of Anaphylactic and Allergic Reactions: An Evaluation of the Role of Histamine in Their Production, Ann. Allergy **2**:457-471, 1944.

anaphylactic shock the histamine content of the blood is increased. The rise roughly parallels the degree of shock. Histamine, however, does not account for the development of incoagulability of the blood, which is a striking feature of shock in the dog. It seems probable that histamine and heparin are liberated simultaneously from the liver as a result of a reaction or a disruption within the hepatic cells. It was suggested that histamine is not the fundamental factor in anaphylaxis or in allergic reactions but is liberated as a consequence of damage done within sensitized cells and that it is this damage to the cell that is the fundamental etiologic factor. The liberation of histamine may be purely incidental. It is not likely that histamine produces the damage. Liberation of histamine, however, may be a lethal factor if the quantities liberated are sufficient and if the animal is sufficiently sensitive to its effects. However, some animals, dogs for instance, may die many hours after the increase in blood histamine has appeared. This suggests that such animals die as a consequence of the cell damage which incidentally liberated the histamine. It seems probable that the fundamental mechanism of anaphylactic reaction lies in the process producing the damage within the cell as a consequence of which heparin and histamine are liberated.

Sherman and Feldman [27] studied the effect of local reactions elicited by specific and nonspecific excitants on the ophthalmic mucous membrane in allergic and nonallergic persons. Their purpose was to ascertain what effects initial specific and nonspecific reactions would have on responses of the ocular conjunctiva to subsequent restimulation with specific and nonspecific excitants. A solution of histamine phosphate was used as the nonspecific excitant, and a solution of ragweed pollen was usually used as the specific excitant. Conjunctival reactions were read in fifteen to twenty minutes, and the reactions were graded primarily on the degree of injection of the ocular and palpebral conjunctivas and caruncle and on the degree of vascular dilatation of the vessels of the limbus and the conjunctiva. The reaction usually subsided in a few hours, and retests were performed three to seven days later. One hundred and fifteen subjects were studied. They were divided into a group of 24 allergic patients who were tested initially with histamine and retested with the same substance, a group of 24 nonallergic subjects who were tested initially and re with histamine, a group of 21 pollen-sensitiv tients who were tested with histamine an tested with pollen, a group of 23 pollen-sen patients who were tested and retested pollen, and a group of 23 pollen-sensitive jects who were tested with pollen and re with histamine. From these experiments it concluded that when the ophthalmic m membrane is stimulated with a nonspecific tant, histamine, and retested later with a sp substance, ragweed, an increased vascular sponse in the form of vascular dilatation occur in approximately 67 per cent of the c Stimulation by histamine followed three to s days later by restimulation with the same stance produces no consistent change in tivity. No change in the vascular res occurs when the procedure is an initial test ragweed followed three to seven days later test with histamine.

Cohen [28] discusses the relation of hista to bronchial asthma. He states that bron asthma always has a distinct pathologic pic regardless of its causes whether intrinsic, trinsic or mixed. The lesions in the bron mucosa and the pathologic appearances r from the reaction to H substance. This subst is pharmacologically indistinguishable from H substance first described by Lewis, and reactions produced are indistinguishable those produced by histamine.

In a study made by Landau and Gay [29] o influence of certain amino acids (arginine histidine) on histamine reactions and ana lactic reactions in intestinal strips of guinea and in intact guinea pigs, it was found arginine or histidine will prevent the effe histamine on the isolated intestinal strip. will also prevent the effect of sheep serum the intestinal strip of a previously sensiti guinea pig. Death from injection of hista can also be prevented by previous admini tion of arginine monohydrochloride, but gave no protection against death in guinea suffering from anaphylactic shock. A 2 per solution of arginine injected intradermally men failed to produce any effect on the outc of intradermal tests with histamine or pollen extracts in sensitive patients, regar

27. Sherman, H., and Feldman, L.: Hypersensitiveness of the Mucous Membrane: Effect of Local Reactions Elicited by Specific and Non-Specific Excitants upon Ophthalmic Mucous Membrane in Allergic and Non-Allergic Individuals, J. Allergy **15**:77-82, 1944.

28. Cohen, M. B.: Bronchial Asthma: Classific Based on Etiological and Pathological Factors, Int. Med. **20**:590-596, 1944.

29. Landau, S. W., and Gay, L. N.: Influen Certain Amino Acids (Arginine and Histidine Histamine Reactions and Anaphylactic Reactions i testinal Strips of Guinea Pigs and in Intact G Pigs, Bull. Johns Hopkins Hosp. **74**:55-76, 1944.

hether it was given together with these sub-
es or injected into the fully developed intra-
al wheal. The authors did not feel that these
o acids would have any clinical application,
the dose used must be high and the effect
uced evanescent.

MÉNIÈRE'S SYMPTOM COMPLEX

llie, Horton and Thornell [30] give an excel-
review of the literature on Ménière's symp-
complex. They present various authors'
s of view on the causes and the treatment
present the characteristic symptoms. Of
al interest was their study based on 25 cases
énière's syndrome in which histamine was
nistered. Eighteen of the patients were men
7 were women. They ranged in age from
65 years with an average age of 46.4 years.
amine diphosphate, 2.75 mg., was adminis-
intravenously in isotonic solution of sodium
ride (250 cc.), a 5 per cent solution of
rose (250 cc.) or an 0.8 per cent solution
otassium chloride at the rate of 20 to 60
s per minute. Histamine was administered
in this manner for three to six days. In
unction with or following the injections, sub-
neous administration of histamine was begun,
dose being gradually increased until the
mal amount was reached. The patient then
inued with the daily injection of histamine
gradually tapered off the dose according to
response to treatment. Audiometric studies
made of the 25 patients before and during
ment. They showed improvement of hear-
in 12 of the 25 patients. In 3 only slight
rovement was noted, in 3 moderate improve-
t occurred and in 6 the improvement was
eable. Improvement was also noticed in
tus immediately following treatment in 14
nts. Twenty-one noted improvement in
go. It was concluded that many persons
Ménière's symptom complex receive definite
fit, shown in improved hearing and less
go and tinnitus when they were treated with
amine.

STUDIES OF THE BLOOD IN ALLERGY

iller [31] in his rhinologic discussion of eosin-
ilia postulates that in allergic reactions when
antigen meets the antibody or reagin there
reaction consisting of edema and release of
histamine due to this local trauma. The bone marrow is probably stimulated, possibly by the histamine liberated, and eosinophils are called forth and pass into the blood stream to the site of reaction. As the eosinophil is a histamine carrier, it seems possible that as a body mechanism to lessen the severity of the reaction eosinophils are taken to the site of reaction to pick up histamine and carry it away. Some histamine may become "fixed" at the site of reaction and thus make it difficult for the eosinophils to take it all away. The number of eosinophils found in the blood stream at any one time will depend on the type of reaction, whether intermittent or constant. This will also influence the number found at the site of reaction. There is great need for further work to be done. One must know, for instance, whether more histamine is always present in nasal polyps as compared with other tissues of the body. This problem must be settled before absolute proof of the true role of the eosinophil in its relation to histamine in allergy can definitely be determined.

An increased number of eosinophils in the blood stream, i.e., more than 6 per cent, occurs in a wide variety of diseases. At the Mayo Clinic Stickney and Heck [32] have analyzed 418 cases in which 6 per cent or more of the leukocytes in the blood were eosinophils. In 33 per cent of the cases of asthma, hay fever and vasomotor rhinitis the eosinophil count was 6 to 10 per cent; in 44 per cent of the cases it varied from 10 to 20 per cent, and in 28 per cent of the cases it was over 20 per cent. They concluded that with few exceptions the degree of eosinophilia is of little importance in differential diagnosis. Allergic disease of the respiratory tract is the most common cause of eosinophilia. Differential counts in which eosinophils accounted for from 6 to 77 per cent of the leukocytes were recorded for this group. In cases of vasomotor rhinitis there may be, of course, a local increase in the number of tissue eosinophils. Other conditions in which eosinophilia was observed include parasitic and nonparasitic infections, blood dyscrasias, dermatoses, cancers, periarteritis nodosa and cirrhosis of the liver. When the clinician encounters eosinophilia, he must consider the common causes, and if none of these can be found in the patient, he must determine whether the degree or the persistence of the eosinophilia is itself a significant factor. There would seem to be no more significance to eosinophilia with a count of over 20 per

. Lillie, H. I.; Horton, B. T., and Thornell, W. C.: ière's Symptom Complex: Observations on Hear- of Patients Treated with Histamine, Ann. Otol., . & Laryng. **53**:717-741, 1944.

. Miller, D.: Significance of Eosinophilia in Rhin- y, Ann. Otol., Rhin. & Laryng. **53**:74-80, 1944.

32. Stickney, J. M., and Heck, F. J.: The Clinical Occurrence of Eosinophilia, M. Clin. North America **28**:915-919, 1944.

cent than to eosinophilia of lesser degree unless possibly the likelihood of periarteritis nodosa or some type of blood dyscrasia being present may be greater. The number of eosinophils varies considerably from day to day and perhaps hourly, a fact which may alter the importance of the findings.

Randolph [33] describes a direct counting chamber method of determining the degree of eosinophilia present in blood. The old method of determining the number of eosinophils in the blood required both a differential white blood cell count and a total leukocyte count. The percentage of eosinophils obtained from the differential was applied to the total number of leukocytes to determine the number of eosinophils per cubic centimeter of blood. This method was not only time consuming but inaccurate because it totaled the errors inherent in the two procedures. Randolph's method consists in using a white cell diluent of phloxine and methylene blue dissolved in equal parts of propylene glycol and water. It permits counting chamber differentiation of eosinophils on the specimen used in determining the total leukocyte count, thus reducing the chance for errors.

ALLERGY AFFECTING THE CENTRAL NERVOUS SYSTEM

Hypnosis apparently has no influence on passive transfer and cutaneous tests. Zeller [34] observed 2 patients, one with bronchial asthma and 1 without any allergy, neither of whom reacted to cutaneous tests with ingestants or inhalants. He sensitized each of them passively by injecting intradermally into both forearms 0.1 cc. of serum from a patient sensitive to ragweed. Twenty-four hours later one of the sensitized areas was given an injection of 0.01 cc. of a 1:500 dilution of ragweed extract. A 4 plus wheal with erythema resulted in fifteen minutes. The control area did not react. Into a sensitized area was injected the same amount and concentration of ragweed extract on the second day. The patients were under deep hypnosis and repeated suggestions were made that cutaneous response would not occur. Within fifteen minutes each patient again had a 4 plus wheal with erythema identical with that of the previous day without hypnosis. The results were rechecked. Two other patients, one with ragweed hay fever and one with bronchial asthma, presented 4 plus reactions to rag extract. Deep hypnosis failed to alter th sponse. Hypnosis and suggestion were tried on a man sensitive to cat and dog da Wheals 1 inch (2.5 cm.) in diameter re from the application of these danders by scratch method. There was no differen the response of the skin before, during or deep hypnosis.

In a discussion of the psychosomatic as of allergy, Karnosh [35] states that the bra capable of a direct and profound reactio protein hypersensitivity and hence this al may cause such conditions as migraine, nière's symptom complex, infantile convul and psychosis. Emotional and mental di bances aggravate an allergic state; mental u may incite angioneurotic edema. Emotions allergies are interlocked, and exacerbation one group enhance the other; they employ same dynamics, one reenforcing the other. good rationale to remove emotional strains f the life of the asthmatic or allergic patient, as much as the offending allergen. Allergy has an effect on the mind of the growing c and is most dangerous to the psyche in the gr ing years. Its effects on bone growth and de development, for instance, are well known, bu effects on the psyche are more difficult to de mine. It may easily form the groundwork hypochondriasis. It was concluded that allergic patient can be adequately evaluated w out considering the personality structure in wh the disease is implanted.

Many cases of Ménière's syndrome, epile infantile convulsions and transient paralysis, example, may be due to allergy of the brain the meninges. Clark [36] describes the aller that may affect the brain, giving local ede and may produce symptoms, therefore, sim lating those of tumor of the brain or cereb edema. Some conditions diagnosed "cyclic vom ing" and "apoplexy" are manifestations of alle of the central nervous system.

As a result of psychiatric studies of clini allergy, Brown and Goitein [37] were able to d cern neurotic and emotional maladjustment 43 per cent of a group of 40 asthmatic patie compared with 10 per cent who showed neuro and emotional maladjustment in a group of control subjects. In a group of 40 nonasthma

33. Randolph, T. G.: Direct Counting Chamber Determination of Eosinophils by Propylene Glycol Aqueous Stains, J. Allergy **15**:89-96, 1944.

34. Zeller, M.: Influence of Hypnosis on Passive Transfer of Skin Tests, Ann. Allergy **2**:515-516, 1944.

35. Karnosh, L. J.: Psychosomatic Aspects Allergy, Psychiatric Quart. **15**:618-625, 1944.

36. Clark, T. W.: Allergy of the Central Ner System, Ann. Allergy **2**:189-196, 1944.

37. Brown, E. A., and Goitein, P.: Psychia Studies in Clinical Allergy, Ann. Allergy **2**:303-1944.

ic subjects, 47 per cent showed neurotic and onal maladjustment. It appears that there pecial type of personality prone to asthmatic cs.

we [38] discusses allergy of the central nervous m and states that it may be manifested by ine, epilepsy, Ménière's syndrome, toxemia psychoneurotic disturbances. The usual gic agent has been some particular food to the patient was sensitive. Diagnosis in cases is made largely by exclusion of certain from the diet.

oore [39] reports a case of unexplained abdom- ain. The patient was a man aged 32 years om isolated paroxysms of abdominal pain been coming on at irregular intervals over iod of twenty-nine years. Electroencepha- phy showed abnormal waves, particularly in ight and left frontal lobes. Anticonvulsant py brought about a cessation of the seizures. patient received extensive clinical study, the explanation offered as to the possible gic basis for the localized epileptic distur- e, expressed by abdominal pain, is that the oral cortex was injured or sensitized by theria antitoxin injected when the patient 9 months old.

arkavy [40] discusses the development or the ression of allergic manifestations during ic endocrine cycles and states that they may tributed to hormonal or autonomic nervous lation, both of which may increase or lower hreshold of cellular response but not initiate Cellular reactions may be induced by cho- gic fibers receiving stimuli from various ces, such as the central nervous system, or ical agents, such as cold and heat. Allergic ions depend on the release of H substance he tissues. It seems, therefore, that the ohormonal system may regulate but not te the hypersensitive type of cellular reac- This control is limited, however, for in s in which sensitization to specific allergens lly developed, the neuroendocrine regulatory tion assumes a minor role.

FOOD ALLERGY

inkel [41] discusses the role of food allergy in rnal medicine and states that every physician should be able to evaluate it correctly in differential diagnosis and be able to advise the patient concerning the nature of the procedures necessary to the evaluation of this problem. The number of foods to which one becomes sensitive increases with age, adults having more food allergies than children. In hay fever the average is five foods, in perennial nasal allergy about seven and in asthma it is above ten per patient. Factors of importance in precipitating food allergy are frequency of use of a given food and infections, especially measles, whooping cough and influenza. These are all dependent on a second factor which he calls "the inherent tolerance for foods." This tolerance varies greatly in different patients, and it predicates the eventual degree of relief which these patients may obtain. A patient who is sensitive to the majority of foods used daily will probably become sensitive to any substituted food. Three criteria indicating food sensitization are listed. If no organic cause has been found, the presence of at least two of the three points will serve as a useful guide.

> 1. The patient, from time to time, will have itching of the nose or the nasopharynx. . . . This sign is seldom absent in food allergy.
>
> 2. At various times the patient will retire free of symptoms and either be awakened out of sleep with an attack of asthma or nasal allergy or develop such upon arising. Again he may be subject to the constant daily level of symptoms and awaken from sleep with a definite exacerbation or have a flare immediately upon arising.
>
> 3. There should be exacerbations of typical symptoms which last two to three days. . . . These criteria are dependent on the fact that practically every allergic individual is sensitive to foods that are used intermittently and will, therefore, produce exacerbations.

Food allergy is classified as being either fixed, that is, constant sensitization, or cyclic. Fixed food allergy is not affected by the frequency of the food in the diet, while cyclic food allergies become clinically evident with continued use of the food and tend to disappear with omission of the food.

Rinkel [42] also discusses the technic and the clinical application of individual food tests. More than 25,000 tests have been performed by his method. Analysis of the data on several hundred patients has shown that the numerical order of foods causing symptoms of sensitivity are wheat, egg, milk, corn, oranges, tomatoes, string beans and Irish potatoes. Therefore, in a patient who failed to react on cutaneous testing or who failed to be relieved of his symptoms when placed on a diet based on positive cutane-

Rowe, A. H.: Clinical Allergy in Nervous Sys- J. Nerv. & Ment. Dis. **99**:834-841, 1944.

Moore, M. T.: Paroxysmal Abdominal Pain: n of Focal Symptomatic Epilepsy, J. A. M. A. 561-563 (Feb. 26) 1944.

Harkavy, J.: Influence of Neurohormonal Regu- ns on Anaphylaxis and Allergy, J. Mt. Sinai Hosp. 65-574, 1944.

Rinkel, H. J.: The Role of Food Allergy in rnal Medicine, Ann. Allergy **2**:115-124, 1944.

42. Rinkel, H. J.: The Technique and Clinical Application of Individual Food Tests, Ann. Allergy **2**:504-514, 1944.

ous tests for foods, wheat should be tested first, because on the basis of probability, it is the food most likely to be a cause of symptoms.

Allergic headache may also be due to food sensitivity. Randolph [43] describes a case of severe headache which was found to be due to sensitivity to milk. The headache was associated with fatigue and a state of altered consciousness. Cutaneous tests for sensitivity to milk were negative.

A case of migraine of thirty years' duration was described by Wolf and Unger.[44] The migraine could be induced by milk and was relieved when milk was omitted from the diet.

Olmsted, Harford and Hampton [45] describe a purified diet composed of amino acids, dextrose and emulsified oil, to which is added a salt mixture and crystalline vitamins. This diet may be of great value in diagnosis in studies of allergic patients, because all foods may be tested and at the same time the patient's nutrition can be maintained.

TREATMENT

Bartlett [46] discusses the ethylene disulfonate treatment of children in the allergic state. The group comprised 247 children ranging in age from 4 months to 16 years. The full dose of 2 cc. of ethylene disulfonate was given at each injection without regard to age. In the younger children the injection was made into the gluteal muscle; in the older ones, into the belly of the deltoid muscle. On the average, 1 dose was given, and the patient then was watched. If another injection was needed, it was rarely given until an interval of at least nine weeks had passed. Of 111 patients with asthma, 56 were completely relieved and 39 practically relieved. Seventy-six patients had hay fever and allergic rhinitis; 39 were completely relieved and 21 were practically relieved. Of 42 patients showing eczema, 33 were completely relieved and 9 partially relieved. Of 13 patients with urticaria, 8 were completely relieved by treatment and 4 practically relieved. Of 5 patients subject to migraine, 4 were completely relieved by treatment and 1 practically relieved. Treatment with ethylene disulfonate gave satisfactory results in 86.64 per cent of the patients treated. It is believed that this treatment marks a definite advance in the therapy of allergy.

Feder and Tribble [47] also state that ethyl disulfonate appears to be worthy of a trial in severe allergic conditions. They are impressed by its potentialities in intractable allergy and multiple sensitivities, especially those related to the basic foods.

Experimentally, however, ethylene disulfonate did not prevent anaphylaxis in guinea pigs. Fisk, Small and Foord [48] describe experiments in which these animals were sensitized by intraperitoneal injection of egg albumin. Ethyl disulfonate did not give sufficient protection against anaphylaxis when the guinea pigs were given a shocking dose of egg albumin.

Ascorbic acid appears to have no effect on cutaneous tests of patients with hay fever. Newbold [49] describes experiments on 8 young adult males who had suffered from periodic attacks of hay fever since childhood. All subjects were cutaneously sensitive to an extract of short ragweed. Vitamin C was given, 1,000 mg. the first day and 500 mg. the second and third days. In some cases 1,000 mg. per day was given for six days. There was no difference in the cutaneous reaction to ragweed before and after ascorbic acid had been given. It is realized that this experiment in itself cannot entirely prove that ascorbic acid can have no clinical value.

Hebold [50] discusses 10 cases of hay fever in which vitamin C was administered. It was found to be an effective form of treatment.

Pelner [51] in a discussion of the importance of vitamin C in bodily defenses presents a case in which the patient was extremely sensitive to ragweed extract. Vitamin C was effective in preventing adverse reactions to injected pollen. The action was thought to take place in the liver where ascorbic acid is one of the substances concerned with detoxification.

43. Randolph, T. G.: Allergic Headache: An Unusual Case of Milk Sensitivity, J. A. M. A. **126**:430-432 (Oct. 14) 1944.

44. Wolf, A. A., and Unger, L.: Migraine Due to Milk: Feeding Tests, Ann. Int. Med. **20**:828-831, 1944.

45. Olmsted, W. H.; Harford, C. G., and Hampton, S. F.: Use of a Synthetic Diet for Food Allergy and Typhoid, Arch. Int. Med. **73**:341-348 (April) 1944.

46. Bartlett, C. L.: Treatment of the Allergic State in Children with Ethylene Disulphonate, Arch. Pediat. **61**:311-316, 1944.

47. Feder, J. M., and Tribble, E.: New Hope for the Allergic? (Use of Ethylene Disulfonate), South. Med. & Surg. **106**:52-53, 1944.

48. Fisk, R. T.; Small, W. S., and Foord, A. G.: Experimental Use of Ethylene Disulfonate in Prevention of Anaphylaxis in Guinea Pigs, J. Allergy **15**: 14-17, 1944.

49. Newbold, H. L.: The Relationship Between Spontaneous Allergic Conditions and Ascorbic Acid: An Experiment Employing Skin Tests and Ascorbic Acid on Subjects with Hay Fever, J. Allergy **15**:385-391, 1944.

50. Hebold, S.: Clinical Evaluation of Ascorbic Acid in Treatment of Hay Fever, J. Allergy **15**:236-239, 1944.

51. Pelner, L.: The Importance of Vitamin C in Bodily Defenses, Ann. Allergy **2**:231-232, 1944.

rickman and Gelbach [52] discuss the symp-tic treatment of seasonal hay fever. Ephe-e and synthetic products of the nature of drine are still the main standbys for the nt who has seasonal hay fever and asthma. padrine hydrochloride and phenylpropanol-e hydrochloride and theophylline (Padro-l) are also useful because they seem to have stimulating side effects on the central ous system than ephedrine. In general, the ded use of nose drops is helpful and affords y patients some relief.

ternberg [53] warns against the abuse of vaso-trictors in hay fever and vasomotor rhinitis. eviews several cases in which nasal obstruc- had persisted with continued use of vaso-trictors. In these cases the condition cleared with five days of nontreatment. Vasocon-tors should be used as a spray only and then more than one to two times in twenty-four rs.

aphthylmethylimidazoline hydrochloride ivine) also causes secondary reactions, which lop in a few hours and eventually become nic. Gollom [54] writes of seeing more than atients during 1943 who became more or less cted to the use of this preparation for the f of nasal obstruction. He concluded that ould be used only under supervision and only a few days at any one time. As an aid to dance of its harmful effects, its sale should limited to persons presenting a physician's scription.

orantil (desiccated kidney and extract of stinal mucosa of hogs containing histaminase) found to be of no benefit in preventing caria following administration of serum. mey, Kriete and Epstein [55] discuss their rvations on the effects of Torantil admin-red to 65 persons who had been treated with toxin for epidemic meningitis. Thirty-six ients were simultaneously treated with his-inase; 29 were not treated. The incidence serum sickness was the same whether aminase was used or not.

Stoesser [56] found that vaccine therapy was of little value in allergies of children. He reviewed 214 cases of allergic rhinitis or bronchial asthma or both. These cases were studied from two to four years, and the study revealed that vaccine therapy was of little value except in those cases in which undenatured bacterial antigens were used. Operative procedures also do not relieve many children who have infections associated with their allergy.

Brown [57] has written an interesting review of the literature on vitamins and allergy for the past five years. He gives the effects pro and con of various vitamins which have been administered for allergic states.

DRUG ALLERGIES

Engelhardt and Derbes [58] discuss allergic reactions to liver extract observed in 2 anemic patients. In the first patient, a young woman suffering from hypochromic microcytic anemia, a local reaction gradually developed at the site of injection on the outer aspect of the arm. The local reaction increased until the area of edema extended to below the elbow. Discontinuance of the liver therapy resulted in complete disappearance of the local reaction within seventy-two hours. The second patient, a woman with pernicious anemia, after transfusion of 500 cc. of citrated blood, was placed on a concentrated extract of liver containing 15 units per cubic centimeter. Almost immediately after the first injection, she felt weak, had difficulty in breathing and lost consciousness. She recovered with injection of epinephrine hydrochloride and supportive treatment. Her history revealed previous similar episodes. Investigation revealed the presence of skin-sensitizing antibodies. The sensitivity to liver may be due to the erythrocyte maturation factor or to some impurity. In regard to allergic reactions, the authors recommend substituting brands of liver extract. However, if the sensitivity is due to the erythrocyte maturation factor, oral liver therapy may be tolerated.

Leftwick [59] describes an intradermal test for the recognition of hypersensitivity to the sulfonamide compounds. This is a method by which positive cutaneous tests may be obtained in

---

Prickman, L. E., and Gelbach, P. D.: Symptomatic Treatment of Seasonal Hay Fever, Proc. Staff ., Mayo Clin. **19**:405-408, 1944.

Sternberg, L.: The Abuse of Vasoconstrictors Hay Fever and Vasomotor Rhinitis, New York J. Med. **44**:1573-1574, 1944.

Gollom, J.: The Problem of Nasal Medication Particular Reference to Privine HCl 0.1%, Canad. A. J. **51**:123-126, 1944.

Toomey, J. A.; Kriete, F. M., and Epstein, H. C.: ntil (Histaminase) in Urticaria Following Serum inistration, J. Pediat. **24**:290-292, 1944.

56. Stoesser, A. V.: Is Vaccine Therapy of Value in Allergies of Children? Journal-Lancet **64**:351-353, 1944.

57. Brown, E. A.: Vitamins and Allergy, Ann. Allergy **2**:156-164, 1944.

58. Engelhardt H. T., and Derbes, V. J.: Allergy to Liver Extract, South. M. J. **37**:31-34, 1944.

59. Leftwick, W. B.: An Intradermal Test for the Recognition of Hypersensitivity to the Sulfonamide Drugs, Bull. Johns Hopkins Hosp. **74**:26, 1944.

patients who have shown hypersensitive reactions to sulfonamide compounds. The material used for the cutaneous test was serum containing a drug level of 2 to 25 mg. of sulfonamide compound per hundred cubic centimeters taken from patients receiving the drug. It was found to be a reliable method of diagnosis in 28 of 30 cases. It was concluded that the sensitizing antigen may be of a sulfonamide–plasma protein combination.

Sulfonamide compounds have been responsible for typical symptoms of bronchial asthma. Randolph and Rawling [60] report 2 cases. In the first patient, status asthmaticus developed on the seventh day following sulfathiazole nasal therapy. There was no history of any previous allergic manifestations. A trial dose of sulfathiazole given one week after the patient had become symptom free resulted in a typical asthmatic paroxysm and a decrease in vital capacity. In the second patient, who was known to be allergic, asthma developed on the first day of a second course of sulfathiazole therapy. A year later a trial injection of 0.5 Gm. of sulfathiazole resulted in diminution of vital capacity but no other symptoms of asthma. It was interesting to note that the eosinophil count dropped from a preinjection percentage of 3.7 to 2.6 at the height of the symptoms and increased to a maximum of 7.4 twenty-five hours after the drug had been taken.

A case of allergy to penicillin is described by Criep,[61] in which massive generalized urticaria developed following the second administration of penicillin. The patient was a man aged 23 who had suppurative arthritis associated with osteomyelitis. He received 200,000 units of penicillin daily for fourteen days, no penicillin for nine days, then 120,000 units of penicillin per day for six days. Immediately on the resumption of the therapy after the nine day rest, massive generalized urticaria developed and persisted until the penicillin therapy was discontinued. The patient had given no history of allergy and had never had urticaria before. An intradermal test with penicillin was positive. Immune bodies, reagins and precipitins were demonstrated in the patient's serum. Direct cutaneous tests with an extract of spores of Penicillium were negative. It seems there is no cross sensitization between penicillin (drug) and extract of spores of Penicillium.

Fungus-sensitive persons are not prone to allergic reactions with penicillin therapy. Feinberg [62] reports his preliminary experiment 10 patients who clinically were mold sens These patients gave positive reactions with tracts of various Penicillia. Intracutaneous tions could be obtained in these patients dilutions as high as 1:1,000,000. A sol containing 25,000 units of penicillin per centimeter tested intracutaneously failed to reactions either in control subjects or in Penicillium-sensitive persons. From these re it seemed that this particular penicillin prep tion could be tolerated by Penicillium-sens patients in doses of at least 500,000 units.

Gabrilove and Kert [63] observed sensitivity thiouracil in 3 of 9 patients with hyperthyroi who were being treated with the drug. had a past history of allergy. The first reac was that of a man aged 55, who after ten da treatment complained of chilliness and ma and showed a temperature of 102.4 F. Mode generalized lymphadenopathy was noted, a day after the febrile rise a diffuse erythema maculopapular rash appeared. Twenty- hours after discontinuance of the drug temperature dropped to normal, and in a days the rash faded. The second reac occurred in a woman aged 30, who was gi 1 Gm. of thiouracil daily. At the end of eighth day her temperature rose to 100.6 F. the next day it was 105. The following da purplish red maculopapular rash appeared on arms. The rash disappeared, and her temp ture dropped to normal following cessation of drug therapy. A week later she was gi 0.2 Gm. of thiouracil. She had a chill, temperature rose to 105.4 F. and the rash appeared on her arms. The third reaction seen in a woman aged 47. Following six days of therapy with 1 Gm. of thiouracil per d leukopenia developed. The white blood count dropped from 6,250 at the beginning treatment to 2,650. Administration of thiou was stopped.

In a study of oils used for intramuscular in tion, Brown, Wilder and Schwartz [64] found sesame and corn oil were superior to peanu cottonseed oil when tested on patients and in and rabbits. Sesame and corn oil were antigenic as determined by the patch test, m quickly absorbed and less irritating to the tis

60. Randolph, T. G., and Rawling, F. F. A.: Bronchial Asthma as a Manifestation of Sulfonamide Sensitivity, J. A. M. A. **126**:166-167 (Sept. 16) 1944.

61. Criep, L. H.: Allergy to Penicillin, J. A. M. A. **126**:429-430 (Oct. 14) 1944.

62. Feinberg, S. M.: Penicillin Allergy: On Probability of Allergic Reactions in Fungus-Sens Individuals, J. Allergy **15**:271-273, 1944.

63. Gabrilove, J. L., and Kert, M. J.: Sensitivity Thiouracil, J. A. M. A. **124**:504-505 (Feb. 19) 194

64. Brown, W. E.; Wilder, V. M., and Schwartz, The Study of Oils Used for Intramuscular Injecti J. Lab. & Clin. Med. **29**:259-264, 1944.

ALLERGY AND WOUNDS

cording to Henry,[65] allergic phenomena play portant role in abdominal wound evisceration. He describes a case in point in which the nt had undergone thyroidectomy with perfect ng. No catgut sutures were used. Six hs later the patient underwent an abdominal ation. On the fifth postoperative day eration occurred. No semblance of the mic catgut remained in the wound. This thought not to be due to defective suture rial, because complete absorption would not occurred in this short time. Twelve addil cases are cited in further illustration. nts of this type do not respond well follow- surgical treatment. They have a low grade , an elevated pulse rate, distention, gas and progressive ileus from the time of ation until evisceration occurs. The wounds lly heal quickly following resuture with non- rbable suture material.

opps [66] describes experiments in which hyper- tivity to catgut was produced in rabbits and ea pigs. Catgut, sheep intestine or sheep m was capable of inducing this hypersensitive . The sensitivity was demonstrated by neous tests, by positive reactions to catgut anted in the anterior chamber of the eye by the demonstration of humoral antibodies vo and in vitro.

isruption of wounds or delayed healing, how- did not occur in rabbits sensitized to catgut. ps,[67] experimenting with rabbits with a pre- n titer for catgut averaging about 1:100, d find no difference in the histologic appear- of the wound, its rate of healing or its gross roscopic appearance when it was compared normal controls. The failure of the tissues ecifically sensitized animals to give rise to gic inflammation on contact with catgut is ably due to the relative insolubility of catgut. local allergic reaction at the site of the nd, however, has been found experimentally lay healing and produce disruption. Hopps,[68] working with rabbits sensitized to horse serum or egg albumin, made laparotomy wounds which were closed either with plain nonboilable catgut or with silk. Immediately after the operation the animals were again given an injection of the specific antigen. Frank separation of the upper layers of the wound developed in some, and others exhibited gaping of the margins of the skin. Most of the animals showed edema and hyperemia of the margins of the wound. The intensity of the reaction tended to parallel the precipitin titer of the serum. Nine days after the operation, biopsy specimens taken at right angles to the line of incision showed a greatly increased number of macrophages, few fibroblasts and a finer reticulum with less collagen than was present in normal control animals. This might account for the decreased tensile strength of wounds of specifically sensitized animals after reinjection of the antigen. Apparently there was a failure of macrophages to mature normally into fibroblasts in these sensitized animals.

Commercial catgut or an extract prepared from catgut does not produce sensitization in rabbits and guinea pigs. Pickrell and Clay [69] implanted catgut in surgical wounds at intervals of one month. Six implants were made, some animals receiving plain catgut and others chromic. There was no evidence whatever of increased local reaction to these implants in these wounds as compared with normal controls.

In other experiments, powdered catgut was deposited in the peritoneal cavity on three occasions at monthly intervals, and skeins of catgut were implanted intraperitoneally at monthly intervals on three occasions. Never was there any evidence of either a local or a general reaction, and the incisions in each instance healed per primam.

Precipitin tests performed at monthly intervals on the serum of the rabbits for antibody production were entirely negative, and intradermal tests for local sensitivity were also negative. The authors analyzed 35 clinical cases of disruption of an abdominal wound and concluded that the primary cause of the disruption was a marked increase of abdominal pressure and could find no evidence of so-called catgut allergy.

ARTHRITIS AND ALLERGY

In a study of 127 cases of arthritis, Turnbull [70] states that food allergy is a basic etiologic factor.

Henry, M. G.: Allergic Phenomena in Relation bdominal Wound Evisceration, Am. J. Surg. **64**: 28, 1944.

Hopps, H. C.: Role of Allergy in Delayed ing and in Disruption of Wounds: I. Antigenicity tgut, Arch. Surg. **48**:438-444 (June) 1944.

Hopps, H. C.: Role of Allergy in Delayed Heal- nd in Disruption of Wounds: II. Effect of Specific tivity to Catgut on Reaction of Tissues to Catgut es and on Healing of Wounds in the Presence of ut Sutures, Arch. Surg. **48**:445-449 (June) 1944.

Hopps, H. C.: Role of Allergy in Delayed Heal- nd in Disruption of Wounds: III. Delayed Healing Disruption Produced by Local Allergic Reaction r Prenomenon), Arch. Surg. **48**:450-456 (June)

69. Pickrell, K. L., and Clay, R. C.: Wound Disruption and Catgut Allergy: An Experimental and Clinical Study, Surgery **15**:333-360, 1944.

70. Turnbull, J. A.: Study of 127 Cases of Arthritis (with Notes on Gastro-Intestinal Features), Am. J. Digest. Dis. **11**:122-130, 1944.

A great many cases of inflammation of the joints may be traced to protein sensitization, either bacterial or food. A diet may easily be selected on the basis of cutaneous tests for protein sensitization which in most instances will relieve an arthritic patient of all or a greater part of his symptoms.

There are also changes in sensitivity to allergenic foods in arthritis. Turnbull [71] discusses 10 cases of arthritis in which the average period of rellef from symptoms was two years and four months; the briefest was one year and one month, and the longest eight years and eight months. A change in diet as predicated by changes in cutaneous reaction to foods completely relieved symptoms of arthritis in these patients.

Hormones evidently play a part in the production of arthritis. Selye and associates,[72] experimenting with rats, found that lesions of joints could be produced, especially in adrenalectomized or thyroidectomized animals, by overdosage with desoxycorticosterone acetate. This polyarthritis histologically resembled that seen in acute rheumatic fever and was frequently accompanied by the appearance of Aschoff bodies in the heart and occasionally by periarteritis nodosa. It was thought that the adrenal cortex may play an important part in the production of rheumatic and rheumatoid conditions in man because of the histologic similarity between those produced in rats with desoxycorticosterone acetate and rheumatic conditions in man.

Urbach [73] suggests that the polyarthritis produced experimentally with desoxycorticosterone acetate may be the clinical expression of an allergy to the hormone of the adrenal cortex. He suggests several experimental tests to prove his assumption, since it is not only important as a theory but is important in the treatment of arthritis.

Hench and Rosenberg [74] report 34 cases of "palindromic rheumatism" studied at the Mayo Clinic. This is a recurring type of arthritis, periarthritis or para-arthritis with pain, swelling and redness resulting in disability of one or more joints. The attacks appear suddenly, last a few hours or days and then disappear leaving articular residues. This condition is probably allergy, although no etiologic factors could found.

MISCELLANEOUS

In an evaluation of cutaneous testing in of allergy, Steele [75] discusses the causative fac in misleading reactions. He expresses the known fact that such tests are of limited va urges "one protein to a test" and does not rec mend the use of combined extracts. Extr should be potent. Dermography may lead false conclusions. Cutaneous testing in stu of urticaria is of no value.

Stoesser [76] states that cutaneous tests are e cially useful in studies of allergy in children, until more research in the laboratory brings diagnostic aids, the greatest advantage must taken of the present methods. Liquid extr furnished in capillary glass tubes were found be the most satisfactory and, of the various me ods of application, the puncture technic on back of the patient yielded the results of grea diagnostic value in determining the cause causes of allergic disease. Localized areas hypersensitivity or hyperirritability of the s may occur and disturb the true pattern cutaneous reactions to allergenic extracts.

In a discussion entitled "Why the Failures the Treatment of Allergy?" Turnbull [77] states allergy can be detected and treated only by with extensive experience and skill in interpre reactions in various types of skin. Many tr however, failures are due to the circumstan that the patient has not followed the doct orders or the diet prescribed, or that the refer physician, when the patient returns to h nullifies or condemns the allergist's direction

Genitourinary symptoms, as frequency, pai urination with burning, tenesmus, nocturi enuresis, ureteral colic, dysmenorrhea, leukorr and so forth, may be due to allergy. Thom and Wicksten [78] present reports of several ca in which patients with disturbances of the geni urinary tract became symptom free on remo of the allergens. Foods were the most comm offenders.

Two cerebrovascular accidents following in tions of epinephrine hydrochloride are repor

71. Turnbull, J. A.: Changes in Sensitivity to Allergenic Foods in Arthritis, Am. J. Digest. Dis. **11**: 182-190, 1944.

72. Selye, H.; Sylvester, O.; Hall, C. E., and Leblond, C. P.: Hormonal Production of Arthritis, J. A. M. A. **124**:201-207 (Jan. 22) 1944.

73. Urbach, E.: Possible Endogenous-Allergic Mechanism of Hormonal Arthritis, J. A. M. A. **124**:731 (March 11) 1944.

74. Hench, P. S., and Rosenberg, E. F.: Palindromic Rheumatism, Arch. Int. Med. **73**:293-321 (April) 1944.

75. Steele, J. M.: Evaluation of Skin Testing Allergy: Discussion of Causative Factors in Misle ing Reactions, Ann. Allergy **2**:17-21, 1944.

76. Stoesser, A. V.: New Interpretations of Al Cutaneous Tests, Journal-Lancet **64**:145-147, 1944.

77. Turnbull, J. A.: Why the Failures in the Tr ment of Allergy? Am. J. Digest. Dis. **11**:363-368, 1

78. Thomas, J. W., and Wicksten, V. P.: Allergy Relation to the Genito-Urinary Tract, Ann. Al **2**:396-403, 1944.

Applebaum.[79] Right hemiplegia occurred in asthmatic patient following a subcutaneous ection of 0.5 cc. of epinephrine hydrochloride. e patient recovered in five weeks except for ht residual facial palsy. The second cerebro- cular accident was similar but much milder. lso resulted from a subcutaneous injection of cc. of epinephrine hydrochloride, given for ef of asthma. These cerebrovascular accidents have been due to cerebral anemia, although h factors as hypersusceptibility, dosage, cumu- ve effect and so forth have to be considered. Two cases of urticaria caused by chlorinated king water have been described by Gut- nn.[80] The urticaria disappeared when the ients drank natural unchlorinated water and ppeared when chlorinated water was given m.

Urticarial reactions have been described by kstein [81] which followed treatment with pooled nan plasma. Reactions of this sort are rare, when they have occurred they were never to the human plasma per se but to antigens m beef, milk and lamb which had been eaten the donor six hours or less before giving the od.

Allergy is an important clinical entity in xico City. Salazar Mallen [82] states that many s of allergy of the asthmatic type are seen. e high altitude is not a cause of allergy, and weed pollen counts have never exceeded 25 ins per square centimeter per day, but dust, thers and food sensitivities are frequent enders.

According to Derbes and Winsor,[83] occupa- al allergy occurs frequently enough to oblige to take a careful history. They list the portant etiologic factors in various occupa- tions and discuss the medicolegal aspect of occupational allergy.

It is interesting to note that air-borne molds are frequent etiologic factors in respiratory allergic diseases. Zink [84] discusses 705 cases observed in San Antonio, Texas, and in an approximate radius of 75 miles. On the basis of reactions to cutaneous tests with the molds and the subsequent clinical course of the patients, it was concluded that air-borne molds are clinically implicated in 25.5 per cent of the patients tested and treated. Alternaria was the most important mold in treatment, while Aspergillus and Penicillium were found to have little clinical significance in the treatment of allergic diseases.

Brown [85] gives an interesting review of the literature on insects and allergy. It is apparent that insects, either their bites or their stings or their emanations, are not a rare cause of allergic disease. Reactions due to stings or bites are easily diagnosed, but those due to emanations are usually much more difficult to discover. However, by history and by testing, many more cases of allergic disease due to insects may be diagnosed.

Orthodontic patients, according to Straub,[86] are frequently allergic. He states that in a series of 104 orthodontic patients who were checked for allergy by scratch tests, intradermal tests and family and personal histories 39.4 per cent were definitely allergic and 12.5 per cent were on the borderline, while 48.1 per cent were free from allergy. Of the 41 allergic patients, 24 had contracted maxillary arches with accompanying protraction of the anterior teeth and retraction of the mandible. The typical adenoid facies is produced by nasal allergy because the ethmoid cells and antrums, as a result of defective aeration, have not kept pace with the development of the patient's face. The child probably is allergic before the age of 6, since this deformation must take place early in childhood.

478 Aquila Court.

79. Applebaum, I. L.: Cerebrovascular Accidents llowing Epinephrine Injections, J. Allergy **15**:392- , 1944.

80. Gutmann, M. J.: Urticaria Caused by Chlorinated nking Water, J. Allergy **15**:395-398, 1944.

81. Dickstein, B.: Severe Urticarial Reactions Due Pooled Human Plasma, Ann. Allergy **2**:327-338, 4.

82. Salazar Mallen, M.: Allergy in Mexico, Ann. ergy **2**:433-437, 1944.

83. Derbes, V. J., and Winsor, T.: Occupational ergy of the Respiratory Tract, Ann. Int. Med. **20**: -264, 1944.

84. Zink, P.: Mold Fungi and the Etiology of Respiratory Allergic Diseases: IV. Skin Reactions to Molds as Correlated with Relative Importance in Treatment, Ann. Allergy **2**:502-503, 1944.

85. Brown, E. A.: Insects and Allergy, Ann. Allergy **2**:235-246, 1944.

86. Straub, W. J.: Frequency of Allergy in Orthodontic Patients, J. Am. Dent. A. **31**:334-342, 1944.

Abstracts from Current Literature

Ear

PSYCHIC DEAFNESS IN CHILDREN. EMIL FROESCHELS. Arch. Neurol. & Psychiat. **51**:544 (June) 1944.

The author tests deafness with a modified accordion of Victor Urbantschitsch by means of which the tones of forty-two whistles forming a scale of six octaves ranging from G-1 to f-4 are introduced into the auditory canal by means of rubber tubes. The ability to hear can be determined by reflex changes, without the cooperation of the patient. The author found 12 psychically deaf children in examining 60,000 children, and he describes the findings in 3 of them in this article.

The evidence presented is conclusive that there are children who have functional deafness and who can be successfully treated.

BEVERLY, Oak Park, Ill. [AM. J. DIS. CHILD.]

TREATMENT OF ACUTE SUPPURATIVE OTITIS MEDIA. LOUIS WESINTEIN and H. B. ATHERSON, J. A. M. A. **129**:503 (Oct. 13) 1945.

Wesintein and Atherson discuss the problem of acute suppurative otitis media and review briefly the methods of treatment, including chemotherapy and the results obtained with penicillin by several otologists. They summarize their own conclusions as follows:

"1. Fifty cases of acute suppurative otitis media, 48 of which occurred as a complication of scarlet fever, were treated with varying doses of penicillin intramuscularly. The external auditory canal was free from exudate in 82 per cent of the patients in less than four and one-half days following institution of therapy. Recurrence of the infection was observed in 16 per cent; these responded well to treatment with larger doses of penicillin.

"2. There appeared to be some degree of correlation between the total dosage of penicillin required to effect a cure and the type of organism producing the middle ear infection. Infections in which the hemolytic Staphylococcus aureus was present alone or in combination with the beta-hemolytic streptococcus seemed to be more resistant to therapy but responded to larger quantities of the antibiotic agent.

"3. Complications of acute suppurative otitis media were reduced to a minimum, and mastoidectomy was only an infrequent necessity.

"4. Secondary infections with gram negative bacteria were well controlled by the local administration of 10 per cent urethane [ethyl carbamate] and 1 per cent sulfanilamide in aqueous solution.

"5. The following regimen is suggested for the treatment of acute suppurative otitis media: intramuscular administration of 15,000 units of penicillin immediately after the appearance of exudate in the external auditory canal and repetition of the same dose every three hours until the aural discharge has been completely absent for seventy-two hours."

GORDON, Philadelphia.

HIGH-TONE DEAFNESS IN SCHOOL-CHILDREN SIMULATING MENTAL DEFECT. MARY D. SHERIDAN, [illegible] M. J. **2**:272 (Aug. 26) 1944.

Five children, whose ages ranged between 9 and [illegible] years, were suspected of being mentally defective. [illegible] examination they were found to have high tone deafness. The author gives the following conclusions and recommendations:

The estimation of the hearing of children by audiometric methods is highly skilled work. The medical staff of every large school should include at least one medical officer (preferably a recognized certifying officer already familiar with the normal standards of intelligence and scholastic attainment) who is adequately trained in audiometry and phonetics. The authorities of smaller schools could send children requiring investigation to the larger centers.

"The hearing of all children over 7 years old who show persistent defects of articulation should be investigated by this trained medical officer. The cooperation of other school medical officers, speech therapists and teachers in referring cases is essential.

"No child with persistent defective articulation should be certified as mentally defective on the results obtained from tests involving language without an investigation of the hearing.

"Accurate diagnosis of high-tone deafness is already possible. The problems of its aetiology and treatment (medical and educational) are matters urgently needing consideration."

BIRDSONG, University of Virginia. [AM. J. DIS. CHILD.]

GIGANTIC CHOLESTEATOMA IN A CHILD. ROBERTO MACHADO ORTEGA, Bol. Soc. cubana de pediat. [illegible] 130 (April) 1944.

A huge cholesteatoma occurring in a 9 year old boy is described. The cholesteatoma had destroyed, by expansion, all the right external auditory canal, the anterior wall of the antrum of the mastoid process and the internal aditus and had invaded the entire mastoid process up to the lateral sinus. The report is followed by a discussion of the pathologic anatomy, the pathogenesis, the symptoms and the treatment. The author asks, "Is there a cholesteatoma diathesis?" and discusses the two types of the lesion, the primary congenital type and the type associated with or due to infection.

KEITH, Rochester, Minn. [AM. J. DIS. CHILD.]

INTRACRANIAL COMPLICATIONS OF MIDDLE EAR INFECTIONS. ANNA SCHOENHOLZER, Pract. oto-rhino-laryng. **5**:113 and 194, 1943.

A survey is made of 138 cases of infection of the middle ear in which intracranial complications occurred in the Berne Clinic from 1925 to 1941. The patients represented 7.7 per cent of all patients seen in this clinic. The complications of cases of acute otitis media outnumbered those of cases of chronic otitis media. The discussion includes the symptoms, the therapy and the prognosis. Epidural abscess is the most frequently occurring complication and the most favorable to the

since cure was effective in 75 cases. Sinal thrombs and otitic septicemia occurred in 30 cases, with in 66 per cent. In 20 cases otitic meningitis rred, in all of which it was fatal. In 13 cases abscess he brain developed, in 7 of which it was cured. The acranial complications usually occurred by direct nsion of the infection from the mastoid process, frequently by way of the blood vessels, through a iscence of bone or by the labyrinthine route. gical intervention was always indicated in these s, and it was supplemented with the administration massive doses of sulfathiazole or Irgamid (N_1-dihylacroyl sulfanilamide). If an abscess of the brain suspected, the particular lobe was punctured and if dence was obtained, the lobe was incised, opened ely and drained by means of a suction pump. The r-treatment consisted in draining off the secretions y.

With the advent of sulfanilamide therapy, the number complications in recent years has decreased, and the gnosis has improved. However, the prognosis ends on the character of the intracranial complica- It undoubtedly is more favorable with epidural ess, sinal thrombosis and abscess of the brain. wever, the prognosis of otitic meningitis is still remely grave.

PERSKY, Philadelphia.

Pharynx

"EXPLOSIVE" OUTBREAK OF HAEMOLYTIC STREPTOCOCCAL TONSILLITIS ON AN R. A. F. STATION. THOMAS S. WILSON, Brit. M. J. **2**:275 (Aug. 26) 1944.

a total camp of 14 officers and 351 airmen, 89 air- were affected during an outbreak of acute hemolytic ptococcic tonsillitis. The patients were acutely ill, wing distinct local and general reactions. The tonsils e red and edematous, with patches of exudate. In y patients the cervical glands were enlarged and der, and in patients without tonsils there was diffuse ryngitis. The temperatures ranged as high as F. The response to the sulfonamide compounds not as dramatic as might have been hoped. In many ents there was a recrudescence of pyrexia around the h day. The blood sedimentation rates were almost iably much raised and remained increased for to five weeks. Convalescence was rather prolonged, g from three to four weeks. As complications, is media occurred in 2 patients, acute carditis in 1 arthritis in 2. Material swabbed from the throats number of patients yielded on culture a growth of emolytic streptococcus which belonged to the Lancefield group A and was serologically type 9. On investigation it was found that one of the cooks, who harbored up A type 9 hemolytic streptococci, had an infection the upper respiratory tract and just before this epiic had been in charge of preparing and distributing k.

There was no correlation between incidence and men g billeted together, but there was a strong correlabetween incidence and men eating in the same mess ; hence it was concluded that this was a food-borne ction. This epidemic is similar to an outbreak of ptococcic sore throat in an American army camp in (1) both outbreaks were food-borne infections and in both epidemics patient to patient infection was imal.

BIRDSONG, University of Virginia.
[AM. J. DIS. CHILD.]

Nose

MAXILLARY SINUSITIS OF DENTAL ORIGIN AND THE MANAGEMENT OF ANTRAL FISTULA. RALPH J. MCQUISTON, Ann. Otol., Rhin. & Laryng. **54**:373 (June) 1945.

McQuiston discusses the development of the maxillary sinus and its relation to the teeth, and why infection of the sinus as a consequence of dental involvement is common. Frequently, breaking through the antral floor during an extraction cannot be avoided, and persistent antral fistula is not uncommon. It is pointed out that antral infections of dental origin are more destructive, because they evade the normal defensive mechanisms of the mucosa by first invading the subepithelial stroma.

A method of treatment of the fistula is described: The fistulous tract is curetted thoroughly. Sliding flaps are prepared by making an incision in the hard palate region about 2.5 cm. in length and 1.5 cm. above and parallel to the alveolar margin, through the soft tissues to the bone. A similar incision is made on the buccal surface of the alveolus, similar to that made in a Caldwell-Luc operation, about 1.5 cm. from the gum margin. The periosteum is then elevated through these incisions on either side of the gum margin down to the opening in the gum margin. The soft tissue with the periosteum is then pulled down on both sides until there is sufficient tissue to close over the bony opening into the antrum completely without being under tension. This is then sutured with a horizontal interrupted mattress suture, heavy black silk being used. This method was used in 8 cases, and the wounds healed promptly.

M. V. MILLER, Philadelphia.

Miscellaneous

TREATMENT OF TYPE B HEMOPHILUS INFLUENZAE MENINGITIS. HATTIE E. ALEXANDER, J. Pediat. **25**:517 (Dec.) 1944.

Early diagnosis and prompt institution of adequate therapy are of signal importance in the outcome of influenzal meningitis, and the expectation of recovery has been shown in previous papers to correlate closely with these factors. At the same time it must be recognized that a few patients recover even after much time has elapsed between the onset of infection and the application of adequate therapy; indeed, some of the patients experience complete recovery in spite of the fact that their meningitis entered what seemed to be a chronic stage. Recovery is attained also by a few of those whose disease appears to include a definitely encephalitic component. An analysis of some of these unusual cases is attempted in the present paper.

When patients are treated early with the combined therapy of sulfadiazine and type-specific rabbit antibody according to the principles outlined, the response has been so consistent that it is possible to predict not only the outcome but the course of recovery. Even when the meningitis progresses so rapidly that the spinal fluid sugar falls to less than 15 mg. per hundred cubic centimeters within twenty-four hours of onset, recovery can be expected to be prompt if sufficient antibody is administered in the initial dose. A favorable course of this kind can be predicted for all patients treated early in the disease with the exception of one small group. An occasional patient exhibits characteristics of a fulminating infection, which is followed by coma within a few hours after the onset of meningitis. Such patients have proved particularly resistant to all forms of treat-

ment—presumably because a significant degree of encephalitis accompanies the meningitis. An example of this form of the disease, in which a favorable outcome was recently obtained, is presented.

Nowadays virtually all of the failures are due to late treatment or to long-standing inadequate treatment. These include the cases of young infants under 7 months of age for whom diagnosis was delayed because of failure of these patients to exhibit easily recognizable signs of meningeal irritation. In older children irreversible injury of the brain may still be encountered for one or both of two reasons—failure to identify the causative organism and too much confidence in the value of sulfonamide compounds when used without the addition of serum.

Thus, one must expect that failures will continue to be encountered, but experience during the last two years has encouraged the discarding of a defeatist attitude and the persistence in energetic treatment of these patients even when ominous signs are at hand. Five unusual cases are presented in detail.

It must be emphasized that the treatment of the chronic form of Haemophilus influenzae meningitis is still in the experimental stage. The term "chronic" has been used to designate the clinical status of the patient rather than the duration of the disease. In this group are classified all those who have exhibited striking rigidity of the extremities as well as of the trunk and who show a preference for the opisthotonic position. While this would be considered the minimal requirement for inclusion in this category, these patients presented additional signs: tremors of extremities and signs caused by damage of cerebral cells.

Two new procedures have been introduced for the chronic cases: the intrathecal administration of heparin and the subarachnoid introduction of air following removal of appropriate quantities of spinal fluid. The former was used in an effort to prevent the formation of additional fibrinous exudate, and the latter, in an attempt to establish communication between the presumably walled-off areas of the subarachnoid space by mechanically breaking up adhesions.

It is the intent, when these patients are seen only after the chronic stage is reached, to use heparin intrathecally as part of the initial treatment and to delay intrathecal administration of serum for several days or until it becomes clear that serum given intravenously is not influencing the meningitis. Intrathecal injection of air will be reserved for patients who fail to respond to serum and heparin administered intrathecally.

AUTHOR'S ABSTRACT. [AM. J. DIS. CHILD.]

THE EXCRETION OF PENICILLIN IN THE SPINAL FLUID IN MENINGITIS. DAVID H. ROSENBERG and J. C. SYLVESTER, Science **100**:132 (Aug. 11) 1944.

Rosenberg and Sylvester administered penicillin in doses of 20,000 to 40,000 Oxford units intravenously and intramuscularly to 8 patients with meningitis. For 6 of these patients the condition had been proved to be meningococcic meningitis. Sixty to one hundred and forty minutes after administration of penicillin the drug was recovered from the cerebrospinal fluid, following lumbar puncture, in concentrations of 0.03 to 0.35 unit per cubic centimeter.

These data suggest that penicillin administered intravenously or intramuscularly in adequate doses may be effective in the treatment of meningitis without supplementary intrathecal therapy.

GUTMAN, Philadelphia.
[ARCH. NEUROL. & PSYCHIAT.]

A CASE OF OSTEOMYELITIS OF THE ODONTOID PRO... OF THE AXIS. F. ARDEN and E. H. DERRICK, M... Australia **2**:487 (Nov. 4) 1944.

The authors report on osteomyelitis of the odon... process of the axis occurring in a child aged 1 y... and 10 months. The pathogenesis was as follo... tonsillitis, purulent cervical adenitis, bacteremia ... metastatic foci in the right lung and in the a... Pneumothorax followed the pulmonary lesion. T... osteomyelitis of the axis led to retropharyngeal abs... as well as to damage of the odontoid process ... general looseness of the neighboring ligaments. Hy... tension of the head at the time of the opening of ... retropharyngeal abscess caused separation of the epi... ysis of the odontoid process, dislocation of the a... compression of the cord and sudden death. The inf... ing organism was Staphylococcus aureus.

GONCE, Madison, Wis. [AM. J. DIS. CHILD.]

CONSIDERATIONS CONCERNING A CASE OF PURU... MENINGITIS DUE TO A HITHERTO UNRECOGNI... ORGANISM. L. VELASCO BLANCO, H. S. VACCAR... and C. RECHNIEWSKI, Arch. am. de med. ... (March) 1944.

A case of purulent meningitis in a 2½ year old g... is presented, in which a peculiar gram-negative ... robic bacillus was isolated from the spinal fluid. T... spinal fluid showed 5,280 cells per cubic centime... of which 97.5 per cent were polymorphonuclear le... cytes; the level of the spinal fluid glucose was pr... tically zero. The patient died in spite of intens... treatment with sulfonamide compounds, which w... given by mouth and intrathecally.

The organism encountered corresponds in morpholo... staining and in cultural and biologic characteristics ... the necrosis bacillus of Schmorl. It differs fr... it in its lack of pathogenicity for the usual experimen... animals.

ABALLI, Habana, Cuba.
[AM. J. DIS. CHILD.]

PURULENT MENINGITIS IN THE INFANT. F. DE ELIZAL... O. R. TURRO and J. GIUSSANI, Arch. argent. ... pediat. **22**:475 (Dec.) 1944.

During the last six years 18 infants with purul... meningitis were treated with sulfonamide compoun... The dosages varied from 0.15 to 1.30 Gm. per kilogra... of body weight, the route of administration being or... intramuscular or intrathecal. The organisms fou... were Pfeiffer bacilli in 9 infants, pneumococci in ... and streptococci in 2. No organism was found in t... remaining 2 infants. The sulfonamide compounds us... were sulfapyridine, sulfathiazole, sulfacetimide a... sulfadiazine. Regardless of the dosage or the route ... administration, all the drugs failed in 16 instanc... The mortality rate was 88.88 per cent; only 2 patie... 1 of them having aseptic meningitis and the oth... meningitis due to Pfeiffer's bacillus, recovered. Su... onamide compounds used early during the primary i... fection were unable to prevent the meningeal compli... tion in 9 children. In all cases complete general ca... was given, including repeated blood transfusions.

The drug level of the spinal fluid was not consiste... with the dosage of the sulfonamide compounds adm... istered.

CASSORLA, Chicago.
[AM. J. DIS. CHILD.]

Book Reviews

anical Allergy: A Contribution to the Study of Pollinosis in Argentina with a Study of Allergenic Flora and Anemopollinometric Count in Río Cuarto and Southeast Cordoba. By José Martorelli. Pp. 184, with 169 illustrations. Buenos Aires: L. E. Ateneo Press, 1945.

Martorelli has made a detailed study of the geographic ribution of the various plants and weeds that may esponsible for allergy in a section of the Argentine ublic. This is an extremely valuable study from standpoint of the botanist and from that of the rgist. Considerable emphasis has been placed on the hods of determining both the type of pollen and its ribution. There are many beautiful photographs trating both the weeds and the microscopic appear- of the pollens. In addition there is an extensive phologic description of each of the possible offending ens, as well as an evaluation of each of the various ts and weeds in its relation to both seasonable and nnial allergy. In the appendix the author gives neral survey of allergy due to pollinosis, summariz- many of the important features, not only from the dpoint of symptomatology but with a view to stress- a careful and thorough history.

lthough this book deals with the flora of one sec- of Argentina, the description of these weeds and ses is extremely useful to allergists throughout the ld, since many of these plants are extremely wide- ad. The book is well written, the matter practi- presented, and its story simply told. The type is l, the photographs are clearcut and descriptive, and paper on which the text is printed is excellent.

e Etiology of Deaf-Mutism, with Special Refer- nce to Heredity. By Harald Lindenov. Trans- ated from the Danish by Axel Anderson. Price 25 kroner. Copenhagen, Denmark: Einar Munksgaard, 945.

n otologist will be satisfied to read in English this ign review of literature on hereditary deafness, mpanied by a study of thirty-two family histories. s the first comprehensive book since the classic by J. Kerr Love, in 1912.

he author is a eugenist who expresses a desire to e, by study of heredity, the differentiation between editary and nonhereditary deaf-mutism. The latter abels, as do other eugenists, "acquired deaf-mutism" ill selected term, since the patients with either type congenitally deaf). An excellent, though brief, chapter covers forty-six previous studies of the eugenics of deafness but singularly overlooks the writings of Alexander Graham Bell, W. A. Turner and J. Kerr Love, who, being workers with the deaf, were most familiar with the subject.

A brief two pages is given to the pathologic anatomy of deafness, the subject which most interests the otologist. But here the literature from any source is too scant.

The difficulty seen in Lindenov's work seems to arise from present inability of otologists to test for and identify types of early deafness. Certainly to some extent the eugenist is dependent on the pathologist and the otologist, and they cannot greatly help in sharp diagnosis. This, then, vitiates many of the conclusions drawn from mendelian theories (as far as deafness is concerned). Undoubtedly, the evidence set forth in this study, as well as in previous studies, confirms the importance of heredity and consanguinity—but it cannot be reduced to valuable expectancy tables. "Mendelism, or any other theory, can do little more than express in new terms what we already know" (Love).

No method of differentiating types of congenital deafness is offered, other than the time-old use of the history of deaf antecedents.

The translation is excellently handled.

News and Comment

OREGON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

The sixth annual spring postgraduate course in ophthalmology and otolaryngology will be held in Portland, Ore., April 15 to 20, 1946. Dr. Algernon B. Reese, professor of ophthalmology, Columbia University, New York, and Dr. Gabriel Tucker, professor of bronchoscopy and laryngology, University of Pennsylvania Graduate School, Philadelphia, will be guest speakers.

AMERICAN BOARD OF OTOLARYNGOLOGY

The next examination of the American Board of Otolaryngology will be held at the Palmer House in Chicago, May 22 to 25. Further information may be procured from the Secretary-Treasurer, Dr. Dean M. Lierle, Iowa City, Iowa.

Directory of Otolaryngologic Societies *

NATIONAL

American Medical Association, Scientific Assembly, Section on Laryngology, Otology and Rhinology

Chairman: Dr. Louis H. Clerf, 1530 Locust St., Philadelphia.
Secretary: Dr. Fletcher D. Woodward, 104 E. Market St., Charlottesville, Va.
Place: San Francisco. Time: July 1-5, 1946.

American Academy of Ophthalmology and Otolaryngology

President: Dr. Gordon B. New, Mayo Clinic, Rochester, Minn.
President-Elect: Dr. Alan C. Woods, Johns Hopkins Hospital, Baltimore 5.
Executive Secretary-Treasurer: Dr. William L. Benedict, 100–1st Ave. Bldg., Rochester, Minn.

American Broncho-Esophagological Association

President: Dr. Carlos E. Pitkin, Carnegie Medical Bldg., Cleveland.
Secretary: Dr. Paul Holinger, 700 N. Michigan Ave., Chicago 11.
Place: Chicago. Time: May 31, 1946.

American Laryngological Association

President: Dr. Harold I. Lillie, Mayo Clinic, Rochester, Minn.
Secretary: Dr. Arthur W. Proetz, Beaumont Bldg., St. Louis.
Time: May 29-30, 1946.

American Laryngological, Rhinological and Otological Society, Inc.

President: Dr. Albert C. Furstenberg, University Hospital, Ann Arbor, Mich.
Secretary: Dr. C. Stewart Nash, 708 Medical Arts Bldg., Rochester 7, N. Y.
Time: May 27-28, 1946.

SECTIONS:

Eastern.—Chairman: Dr. Oram R. Kline, 414 Cooper St., Camden, N. J.
Southern.—Chairman: Dr. Verling K. Hart, 106 W. 7th St., Charlotte, N. C.
Middle.—Chairman: Dr. Carl H. McCasky, 608 Guaranty Bldg., Indianapolis.
Western.—Chairman: Dr. Aubrey G. Rawlins, 384 Post St., San Francisco.

American Otological Society

President: Dr. Gordon Berry, 36 Pleasant St., Worcester, Mass.
Secretary: Dr. Isidore Friesner, 101 E. 73d St., New York.
Time: May 31-June 1, 1946.

American Otorhinologic Society for the Advancement of Plastic and Reconstructive Surgery, Inc.

President: Dr. Alfred Schattner, 115 E. 61st St., New York.
Secretary: Dr. Norman N. Smith, 291 Whitney Ave., New Haven, Conn.

* Secretaries of societies are requested to furnish the information necessary to keep this list up to date.